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**The Impact of Cognitive Dysfunction Upon the Non-Metastatic Colorectal Cancer  
Patient's Psychosocial Adjustment and Quality of Life**

**by**

**Jacqueline Galica**

**A Thesis  
Submitted to the Faculty of Graduate Studies  
through Nursing  
in Partial Fulfillment of the Requirements for  
the Degree of Master of Science at the  
University of Windsor**

**Windsor, Ontario, Canada**

**2008**

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## ABSTRACT

This study associated chemotherapy-related cognitive impairment with Psychosocial Adjustment and Quality of Life (QOL) in seventy-four colorectal cancer patients. Assessments included the Cambridge Neuropsychological Test Automated Battery (CANTAB), Psychosocial Adjustment to Illness Scale – Self Report Version (PAIS-SR), and Functional Assessment to Cancer Therapy – General Version (FACT-G).

The sample consisted of 4 groups: A & C (stage III/ high-risk II), with A assessed pre-chemotherapy and C post-chemotherapy; and groups B & D (stage I/II) who did not require chemotherapy, with B assessed post-operatively and D 6-months post-operatively. A statistically insignificant negative association was found between CANTAB and PAIS-SR results. The association between PAIS-SR and FACT-G was also negative, was highly significant, and indicates that as psychosocial adjustment improves, so does QOL.

This study suggests that cognitive changes do not influence patients' relationships and functional roles, which are strongly associated with QOL.

Dedication

For Kevin

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## Chapter 1

### *Introduction*

#### *An Overview of Colorectal Cancer and Psychosocial Adjustment*

The Canadian Cancer Society (CCS) and the National Cancer Institute of Canada (NCIC) estimate that 166,400 new cases and 73,800 deaths from cancer will occur in Canada this year. Of these, 21,500 new cases of colorectal cancer will be diagnosed, and 8,900 will die from the disease (Canadian Cancer Society/National Cancer Institute of Canada, 2008). Colorectal cancer incidence has remained relatively stable for the past eight years, whereas mortality rates have continued to decline since 1979 (by 1.7% in females and by 1.3% per year in males). These findings are attributed to increased attention toward population screening programs, and recognition of colorectal cancer's modifiable risk factors (Canadian Cancer Society/National Cancer Institute of Canada, 2005), as well as improvements in chemotherapy (Canadian Cancer Society/National Cancer Institute of Canada, 2008), all of which have led to a longer duration of living with the illness.

Although chemotherapy has continued to be a standard treatment for colorectal cancer over the last 40 years (Midgley & Kerr, 2000), it is only within the past two decades that the impact of treatment upon the patient has been addressed within a holistic framework. Chemotherapy is often used alone or in combination with radiation for the post-operative adjuvant treatment of colorectal cancer (Midgley & Kerr, 2000). Physical side-effects of chemotherapy are well known and managed by the health care team, but other side-effects, such as changes in cognitive function, have only recently been acknowledged and are consequently understudied. The needs of the colorectal cancer patient are multi-factorial and therefore complex.

Nursing has a professional responsibility to care for the multi-dimensional needs of clients. In outlining the competencies related to their standards of practice, the College of Nurses of Ontario (CNO) directs Registered Nurses to collaborate with clients in a holistic assessment addressing their physical, emotional, psychological, cognitive, social, spiritual, developmental, cultural, and educational needs (College of Nurses of Ontario, 1999, p. 15). Other organizations that identify the holistic responsibilities of nurses are the Canadian Nurses Association (2002) and the American Holistic Nurses' Association (1994). Thus stated, holistic care is a necessary component of quality nursing care which benefits the lives of colorectal cancer patient care.

Nursing is not the only health profession interested in caring for the multi-dimensional needs of cancer patients. In the 1980s, the Canadian Association of Psychosocial Oncology emerged with the multi-disciplinary intention to research and care for the psychosocial needs of cancer patients. They characterize psychosocial oncology as that which strives to understand and treat the "social, psychological, emotional, spiritual, quality-of-life and functional aspects of cancer" (Canadian Association of Psychosocial Oncology, 2005). From this definition, it is clear that the aims of psychosocial and holistic care are similarly multi-dimensional in their scope.

Within the oncology literature, studies have demonstrated the impact that a cancer diagnosis and treatment have upon a person's psychosocial adjustment (de Paula Lima, 2005; Gilbar & De-Nour, 1989; Kelman, 1997; Wolberg, Romsaas, Tanner, & Malec, 1989). In a phenomenological exploration of a colorectal cancer diagnosis, Taylor (2001) described the participants' most distressing theme of feeling that they were on their own. This experience was generated by the subjects' personal reflection of themselves, values, beliefs and accomplishments, as well as their desire to protect loved ones from details of

the diagnosis and treatment. Additionally, psychological distress related to the frequency of existential thoughts has been found to occur in over 93% of those diagnosed with colorectal cancer (Klemm, Miller, & Fernsler, 2000). The differences in psychosocial adaptation between cancer patients and healthy controls is made clear by Wolberg et al. (1989) who claim that the issues with adjustment persist for up to 16 months after a diagnosis. Furthermore, it is the quality of attention given to cancer patients' psychosocial needs which is correlated with higher patient satisfaction as opposed to the duration of time spent with patients giving them numerous resources (Walker, Ristvedt, & Haughey, 2003).

The studies outlined above confirm the impact that a cancer diagnosis has upon one's psychosocial adjustment. However, the influence that specific symptoms related to cancer treatment have upon a person's psychosocial adjustment remains unclear. Of particular interest, is the symptom of cognitive dysfunction related to chemotherapy. While it is well documented that cognitive decline has been associated with chemotherapy treatment, particularly for breast cancer, there are few studies relating chemotherapy-induced cognitive dysfunction and psychosocial issues. This research will attempt to fill this void in the oncology literature.

#### *Theoretical Framework*

The framework used to guide this research is the Theory of Unpleasant Symptoms developed by Lenz, Suppe, Gift, Pugh, and Milligan (1995). The theory began its development when three of the investigators began simultaneously working on two different concepts representing unpleasant symptoms. Initially, two of the investigators collaborated about their studies of women's fatigue at different phases of the childbearing process, and then another set of two investigators realized that they were conceptualizing

different concepts in similar terms (Lenz et al.). Collectively, these researchers began to examine other similar concepts in hopes that they could be formed into a general framework. Thus began the formulation of The Theory of Unpleasant Symptoms.

The assumption behind the theory is that it can guide research and practice for any number of symptoms since symptoms share many commonalities (Lenz, Pugh, Milligan, Gift, & Suppe, 1997). The theory proposes that three categories of influencing factors (physiologic, psychologic and situational) relate to each other and may individually or collectively affect the predisposition or manifestation of an unpleasant symptom (Lenz et al.). In outlining examples of each factor, Lenz et al. describe physiological factors as normal functioning body systems, existence of pathology or level of energy; psychological factors as mental state or mood, affective reaction to illness or degree of uncertainty about symptoms; and situational factors as aspects of the social and physical environment that may affect the person's experience and reporting of symptoms.

The theory's central concept, the unpleasant symptom(s), is experienced by the patient and is defined by Hegyvary (as cited in Lenz et al., 1997) as the "perceived indicators of change in normal functioning as experienced by the patients". One symptom may occur at a time, although it is more common for more than one symptom to transpire simultaneously, usually in a catalyzing manner (Lenz et al.). Each symptom is multi-dimensional, varying in intensity (severity or strength), time (frequency or duration), distress (irritating or bothersome), and quality (a subjective description) (Lenz et al.).

The outcome of the symptom impacts the person's functional and/or cognitive performance. Functional performances may include physical activities, social activities,



interaction and role performances, whereas cognitive performances include concentrating, thinking and problem-solving (Lenz et al., 1997).

The original, or in-process Theory of Unpleasant Symptoms (1995), posited unidirectional relationships of the influential factors on symptoms, and symptoms on performance. In their updated model, Lenz et al., (1997) theorize that relationships among the concepts may be more reciprocal. They propose that symptoms may affect the influencing factors, and that performance outcomes may shape the symptom experience as well as the influential factors. Figure 1 illustrates the relationships between the concepts within The Theory of Unpleasant Symptoms.

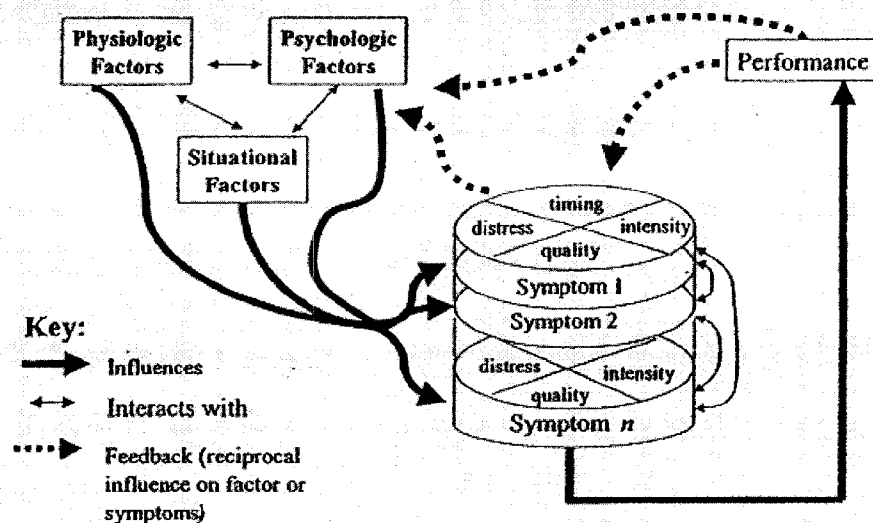


Figure 1. A diagram depicting the conceptual relationships within the Theory of Unpleasant Symptoms.

Note. From "The Middle-Range Theory of Unpleasant Symptoms: An Update," by E. R. Lenz, L. C. Pugh, R. A. Renee, A. Gift and F. Suppe, 1997., *Advances in Nursing Science*, 19(3), p. 14-27. Copyright 1997 by Wolters Kluwer Health. Reprinted with permission.

The Theory of Unpleasant Symptoms was based on inductive and deductive research, and analyses have shown support for the model in relation to maternal health, and dyspnea (Lenz et al., 1997). The theory has recently begun to appear within the oncology literature and has shown support for the relationship between disease and treatment-related symptoms upon performance (Robinson, Bradway, Nuamah, Pickett, & McCorkle, 2008; Thompson, 2006), and that this relationship was strengthened when symptoms were clustered (Thompson). In using the theory to explore lymphedema symptoms of breast cancer patients, Ridner (2004) strengthened the theory's claim that symptoms are multi-dimensional, resulting from combined influencing factors, and that interventions targeted toward one factor is inadequate in relieving the symptom. However, Redeker, Lev and Ruggiero (2000) suggest that the effect of symptoms (fatigue and insomnia) on quality of life decreased in the presence of psychological factors (depression and anxiety). Due to this difference, and due to the small numbers of oncology research projects that have explored the relationships within the Theory of Unpleasant Symptoms, further exploration into cancer and treatment related symptoms is needed in relation to the theory to more clearly illustrate the relationships among these concepts.

The concepts explored in this research (cognitive impairment, psychosocial adjustment and quality of life) can easily be related within the Theory of Unpleasant Symptoms. The symptom of cognitive impairment that is precipitated by chemotherapy can affect the ability to perform cognitive tasks. It is these cognitive tasks, or performance, that objectively indicate that the symptom is present. A poorer performance in cognitive abilities can affect mood, reaction to illness or uncertainty, known as psychological factors within the theory. A poorer performance can also affect the social

environment in which one is involved (situational factor) or their level of energy (physiological factor). These psychological, situational and physiological factors encompass many other issues that are comparable to the concepts of psychosocial adjustment and quality of life, for which there are validated tools to use. Finally, the effects of the disruptions in these influencing factors can manifest the distress, intensity, timing and quality of the original symptom, cognitive impairment.

For the purposes of this research, it is the impact of performance outcomes (chemotherapy-induced cognitive impairment) upon the influencing factors (psychosocial adjustment and quality of life) that will be explored. In order to explore these relationships, a review of these concepts within the scholarly literature will be conducted. An investigation into the oncology literature will take place, with a particular emphasis upon the experiences involving colorectal cancer patients.

## Chapter II

### *A Review of the Literature*

#### *Relationships Between Chemotherapy and Cognitive Dysfunction*

##### *The magnitude of cognitive dysfunction associated with chemotherapy*

Within the oncology literature, there is growing evidence showing the effects of chemotherapy upon cognitive function. Most of the research in this area has investigated women with breast cancer who received adjuvant treatment, and show that as many as 16-75% of them show moderate to severe cognitive impairment in a variety of manifestations (Ahles et al., 2003; Brezden, Phillips, Abdoell, Bunston, & Tannock, 2000; Schagen et al., 1999; Tannock, Ahles, Ganz, & van Dam, 2004). In fact, as many as 32% of people receiving high-dose chemotherapy and 28% of those receiving standard or adjuvant

therapy objectively display post-treatment cognitive impairment (Schagen et al., 1999; van Dam et al., 1998).

In their comparison of women with breast cancer receiving high-dose chemotherapy, standard chemotherapy or local radiation therapy, van Dam et al. (1998) found that women who received standard chemotherapy were 3.5 times more at risk (CI 95%) of developing cognitive impairment as compared to those who received local treatment. Other studies conducted in non-brain tumor populations have shown similar results indicating that people who are treated with systemic chemotherapy experience greater cognitive disturbances than those treated with more localized modalities (Schagen et al., 1999; Ahles et al., 2005). These studies demonstrate the impact that chemotherapy has upon the cancer patient's cognitive function. The surplus of research in breast cancer populations has produced results that are difficult to generalize. Therefore, studies within other cancer groups is necessary.

#### *The manifestations of chemotherapy-induced cognitive dysfunction*

In order to have a detailed discussion about the relationship between cognitive dysfunction and chemotherapy, it is imperative to understand what is meant by cognitive dysfunction. Within the research literature, cognitive disturbances vary according to treatment, but are commonly manifested by subtle declines in memory, concentration, mental foginess, and ability to stay focused or organized (Ahles & Saykin, 2001; Iconomou, Mega, Koutras, Iconomou, & Kalafonos, 2004; Taillibert, Voillery, & Bernard-Marty, 2007). Studies have captured both subjective and objective details about these cognitive disturbances, which have (Vardy, 2007) and have not found relationships to each other (Iconomou et al.; van Dam et al., 1998). Self-reports from patients who received chemotherapy demonstrate moderate or highly disruptive problems with

memory or concentration, which is statistically significant over patients in a control group (Schagen et al., 1999; van Dam et al.).

*The duration of chemotherapy-induced cognitive side-effects*

The exact duration of cognitive dysfunction lasting beyond the treatment period is unknown; however, longitudinal studies are ongoing. Initial studies in this area show that cognitive dysfunction noticed at the completion of treatment can go on for as long as two years (Bender et al., 2006) and even ten years after chemotherapy is completed (Ahles et al., 2002). It is interesting to note that the majority of patients in this study received only one standard-dose chemotherapy regimen, which presents many questions about more highly cytotoxic regimens or investigational drugs.

*The mechanisms of chemotherapy-induced cognitive dysfunction*

The exact mechanisms of chemotherapy-induced cognitive dysfunctions are currently unknown, and continue to be studied. One possible explanation is that chemotherapy causes neurotoxic damage (Saykin, Ahles, & McDonald, 2003), and damage can be dependent upon treatment type (Bender et al., 2006; Scheibel, Valentine, O'Brien, & Meyers, 2004) and dose (Taillibert et al., 2007). Another possible explanation is having a genetic predisposition toward cognitive impairment. Ahles et al. (2003) showed that those who received chemotherapy and were carriers of the apolipoprotein E e4 allele tended to score lower on various neuropsychological tests than survivors with other alleles of lipoprotein. Other explanations could be related to the function of cytokines, which are small proteins within the body used to regulate immunity and inflammation, even functioning as growth factors (Fox, 1996). Studies have shown that elevated cytokine levels increase lethargy and impair learning (Banks, Farr, & Morley, 2003; Slaviero, Clarke, & Rivory, 2003). However, when exploring the IL-1 $\beta$ ,

IL-2, IL-4, IL-6, IL-8, IL-10, IL-12, TNF $\alpha$ , TNF $\gamma$  and GM-CSF levels in colorectal cancer patients, Vardy (2007) found that none of the cytokines were significantly associated with either objective or subjective cognitive impairment. Physiological changes occurring in the brain after receiving chemotherapy is another plausible cause of cognitive impairment in cancer patients. When using neuro-imaging techniques to explore the cerebral anatomy of patients who received chemotherapy in relation to healthy controls, a reduction in gray matter was found throughout the brain, hippocampal volume loss existed, and decreased metabolic activity in the frontal areas of the brains of cancer survivors who received chemotherapy was found (Reminger et al., 2004; Saykin et al., 2003; Silverman et al., 2003). Other research is exploring mechanisms of chemotherapy-induced cognitive function in animal models, but has not yet shown similar results in clinical research.

*Potential confounders to chemotherapy-induced cognitive dysfunction*

A cancer diagnosis and treatment has the ability to change a person's emotional and psychological stability. However, studies suggest that the incidence of depression in cancer patients range from being no different than those without cancer (Keating, Norredam, Landrum, Huskamp, & Meara, 2005) to greater than forty percent, with the greatest rates of psychiatric morbidity being found in those receiving palliative treatment (Fallowfield, Ratcliffe, Jenkins, & Saul, 2001). Jenkins et al. (2006) found that patients with early breast cancer who exhibited psychological distress, reported significantly more cognitive failures. Within the oncologic literature, a significant correlation between objective cognitive performance and depression or anxiety has not been found (Vardy, Rourke, & Tannock, 2007).

However, the relationships between cognitive changes and emotional distress, such as anxiety or depression, have been extensively studied and reported outside of the oncology literature. Relative to states of anxiety in case-control studies, cases were found to have significant impairments in episodic memory and functioning over controls (Airaksinen, Larsson, & Forsell, 2005) and more severe symptoms of anxiety were negatively associated with cognitive function (Bierman, Comijs, Jonker, & Beekman, 2005). More extensively studied is the relationship between depressive states and cognitive dysfunction. In their review of studies exploring cognitive deficits in depression, Austin, Mitchell, and Goodwin (2001) found mnemonic deficits and executive impairments occurred independently of age, or depression severity or subtype. In case-control studies exploring depression and cognitive dysfunction, cases were consistently found to perform worse in functions of memory, response suppression and multi-tasking (Austin et al., 1999; Channon & Green, 1999) and impairments of memory and executive function were found to continue despite remission of a depressive episode (Rubinsztein, Michael, Paykel, & Sahakian, 2000). Therefore, it is important for studies reviewing the causes of chemotherapy-induced cognitive dysfunction to consider a variety of other factors apart from the chemotherapy treatment itself.

Cancer related fatigue exists and may last well beyond the treatment period (Tchen et al., 2003). A strong association between fatigue and perceived cognitive impairment has been found, but has not been evident when exploring fatigue and objective neuropsychological testing (Ahles et al., 2002; Schagen et al., 1999; Tchen et al.; van Dam et al., 1998).

In most chemotherapy protocols, it is standard for other medications to be prescribed in order to alleviate many of the unwanted side effects of chemotherapy.

These medications are often steroid based, which on their own have been found to affect a person's cognitive performance. Glucocorticosteroids have been shown to decrease capillary permeability of the blood brain barrier and decrease cerebral blood flow (Saykin et al., 2003). Newcomer, Craft, Hershey, Askins, and Bardgett (1994) conducted a four day trial of double-blind, placebo controlled dexamethasone study in normal adults to determine the impact of the treatment upon cognitive function. They found impairment of verbal declarative memory performance after only a four day treatment of relatively low-dose of dexamethasone. More recently, similar findings have been found in healthy adults receiving hydrocortisone therapy (Newcomer et al., 1999). Collectively, these studies should caution both clinicians and researchers to other potential contributors of change in cognitive function.

*The objective measurement of cognitive dysfunction*

There are a number of tools available to measure changes in cognitive function. Neuropsychologists recommend a comprehensive battery of tests to best assess cognitive function, but vary in opinion of what tests, and how many (Vardy et al., 2007). Therefore, the ideal method of measuring cognitive function would evaluate a number of domains, be brief and non-stressful for patients, independent of language skills, free of practice effects and sensitive to changes occurring over time (Robbins, James, Owen, Sahakian, McInnes, & Rabbitt, 1994; Tannock et al., 2004; Vardy, 2005, Vardy et al., 2007). A tool to evaluate cognitive function that contains all of the above characteristics does not exist (Vardy, 2005), so the measurement of such functioning in research studies is widely varied.

In their praised review of cognitive function and chemotherapy studies, Vardy et al. (2007) found that studies are inconsistent in describing types of cognitive function,



although the commonly affected domains include complex attention/concentration, verbal and visual memory and processing speed. Since most neuropsychological tests report their results as Z or T scores, a definition of cognitive dysfunction is commonly based on the cutoff scores for the various tests. Within their review, Vardy et al. acknowledge that subtle impairment is most commonly defined as greater than 1 SD below the mean, while higher levels of dysfunction lie between 1.5 to 2 SD below the mean. It is also difficult to precisely define cognitive impairment because batteries contain several individually scored tests. That said, it is a common practice for impairment to be determined on more than one test to classify a person as cognitively impaired. This results in a variable objective definition of cognitive impairment which makes comparisons between studies very difficult.

To overcome the problem of using multiple tests to define cognitive impairment, Global Deficit Scores (GDS) are commonly used to define objective cognitive impairment. Heaton et al. claim that the GDS considers both the number and severity of deficits an individual performs on a battery of tests, while paying less attention to performances that lie within and above normal limits (as cited in Carey et al., 2004). The demographically corrected T-scores of individual tests are converted to a deficit rating, ranging from 0 (no impairment) to 5 (severe impairment) (see Table 1). These ratings are then averaged to create a Global Deficit Score (GDS) for the battery completed by each participant (Carey et al., 2004). A GDS of greater than or equal to 0.5 means that a mild impairment was averaged over 50% of the tests. Although a GDS of 0.5 has been suggested as the cutoff for detecting cognitive dysfunction in HIV patients, no optimal cutoff for cancer patients has been determined.

Table 1: A Conversion Table for Transforming T-Scores into Deficit Scores (Carey et al., 2004)

T-Score	Deficit Score	Impairment Descriptor
$\geq 40$	0	Normal
39-35	1	Mild
34-30	2	Mild to Moderate
29-25	3	Moderate
24-20	4	Moderate to Severe
$\leq 19$	5	Severe

Within the oncology literature, the High Sensitivity Cognitive Screen (HSCS) has been frequently used to measure and assess changes in cognitive function. Although valid, reliable and sensitive to the detection of subtle cognitive impairment (Serper & Allen, 2002), the HSCS has been recently found to have limitations within cancer research. Such limitations include the acknowledgement of a practice effect with repeated measures that may underestimate the level of cognitive dysfunction in patients as compared to the initial evaluation (Mar Fan et al., 2005), and that the HSCS may not be sensitive enough to detect subtle cognitive impairment (Vardy, 2005). Also a limiting factor is the tool's inability to be used with participants with an inadequate knowledge of the English language, since the recipients of care at urban cancer centres include many people from non-English speaking cultures.

Another tool used to assess impairment in cognitive function is the Cambridge Neuropsychological Test Automated Battery (CANTAB). Although not extensively used within oncology research, the CANTAB batteries have been validated and used to assess cognitive performance in a variety of neuropsychiatric disorders in comparison to healthy controls (Lowe & Rabbitt, 1998; Luciana, 2003; Robbins et al., 1994). The main advantage of the CANTAB is that it uses a touch-screen computer, which offers the

research subject an unbiased and highly consistent mode of presentation, without necessitating a strong command of the English language. It also has the advantage of incorporating a wide variety of tests using both frontal and temporal functions (Lowe & Rabbitt, 1998; Robbins et al., 1994). The CANTAB measures visual memory, working memory and planning, sustained attention, motor skill, information processing and recognition memory via the following tests: Motor Screening (MOT), Affective Go/No-Go (AGN), Big/Little Circle (BLC), Delayed Matching to Sample (DMS), Intra-Extra Dimensional Set Shift (IED), Match to Sample Visual Search (MTS), Paired Associates Learning (PAL), Pattern Recognition Memory (PRM), Reaction Time (RTI), Rapid Visual Information Processing (RVP), Stockings of Cambridge (SOC), Spatial Recognition Memory (SRM), Spatial Span (SSP), Spatial Working Memory (SWM), and Verbal Recognition Memory (VRM) (Cambridge Cognition Limited, 2004). Further details outlining these tests can be found in Appendix E. Although extremely comprehensive and easily administered and completed, the CANTAB has limitations in how long it takes to complete (2 hours 30 minutes in entirety), and requires the additional costs of obtaining software, hardware and administrator training (Cambridge Cognition Limited, 2004; Collie, Darby, & Maruff, 2001).

*Studies of prevention and coping with chemotherapy-induced cognitive dysfunction*

As previously outlined, the exact mechanisms of chemotherapy-induced cognitive dysfunction are unclear. As such, there are a minimal number of reports that have studied interventions to prevent or enable patients to cope with such cognitive dysfunction, and those studies have failed to show strong results. For example, a study of breast cancer patients receiving adjuvant or neoadjuvant chemotherapy were randomly assigned to receive epoetin- $\alpha$  or standard treatment over the course of their chemotherapy treatment,

and were compared for changes in cognitive function, quality of life and fatigue. When cycle 4 treatment scores were compared to baseline, the epoetin- $\alpha$  group had a mean change from 1.3 to -3.3 in their cognitive performance with the control group demonstrating a smaller mean change of 0.3 to -2.4 (O'Shaughnessy, 2002; O'Shaughnessy et al., 2005). Note is made that a negative change indicates improved function, and that there were no changes in mean changes from baseline to the 6-month assessment of cognitive function (O'Shaughnessy et al., 2005).

There is little anecdotal information found within the oncology literature to guide practitioners in developing interventions to enable cancer patients to cope with cognitive dysfunction. However, at a cognitive workshop, breast cancer survivors discussed the cognitive problems following treatment as well as coping strategies employed (Tannock et al., 2004). Such strategies include avoiding multiple simultaneous tasks, decreasing workload and increasing rest periods. Other than this, little is known about the impact of cognitive dysfunction upon the cancer patient. It is for these reasons that further studies are necessary to understand this impact in order to guide practice, and to assist clients through the development of holistically sensitive interventions.

### *Psychosocial Adjustment*

#### *A history of the term*

In the mid-1900s, psychiatrists began to recognize a relationship between patients' physical illness and their coping and social supports (Derogatis & Fleming, 1996). It was in the 1950s that preliminary attempts were made to measure these relationships, which was then termed psychosocial adjustment. Since that time, few psychometric instruments have been developed to measure psychosocial adjustment despite the literature outlining the strong psychosocial component that characterizes the etiology, course and outcome of

chronic medical conditions, such as cancer (Derogatis & Derogatis, 1990; Derogatis & Fleming, 1996).

*Psychosocial adaptation or adjustment: What's the difference?*

The terms psychosocial adaptation and psychosocial adjustment are both found in the literature and are often used interchangeably. It is for this reason that a brief review of these terms will be provided.

In relation to the person coping with a traumatic life event, Livneh and Antonak (1997) describe psychosocial adaptation as a gradual process that assimilates the changes occurring in the individual's body, body image, ego, self concept and person-environment interactions. Within the process toward adaptation, adjustment is the clinical and subjective final phase of the process, expressed in terms of reaching and maintaining psychosocial equilibrium; achieving reintegration; striving to reach life goals; positive self-esteem, self concept and self-regard; as well as experiencing a positive attitude toward the self, others and one's disability (Livneh & Antonek, 1997).

In further reviewing the literature, there were no other definitions that clearly segregate the meaning of adaptation from adjustment. Therefore, for the purposes of this research, the term adjustment will be used herein and will be the concept of interest.

*A varying definition*

Upon reviewing the scholarly literature, it is evident that the concept of psychosocial adjustment is used variably despite being studied for a number of years. Friedman, Baer, Lewy Lane, and Smith (1988) identified that the definition and measurement of psychosocial adjustment has been attempted in three ways: by using clinical indicators such as mood states to infer psychosocial adjustment; by using the behaviours correlated with mood states, such as sleeping or eating patterns, to infer

psychosocial adjustment; and by measuring the impact of specific roles and relationships as an implication of psychosocial adjustment.

There is consensus that psychosocial adjustment is a subjective, multi-dimensional concept (Bishop, 2005; Derogatis & Fleming, 1996; Linveh & Antonak, 1997; Shapiro, Lopez, Schwartz, Braden, & Kurker, 2001). Some research studies define the concept using a variety of psychometric tools to collectively measure varying interpretations of psychosocial adjustment. Such tools have included the measurement of the concepts of subjective well-being, self-concept, coping, life goals and satisfaction, psychological consequences such as depression, distress and worry, as well as inter-relational issues such as communication problems, social support and role functioning (Carlsson, Bjorvatn, Engebretsen, Berglund, & Natvig, 2004; Derogatis & Derogatis, 1990; Felder-Puig et al., 1998; Heim, Valach, & Scaffner, 1997; Shapiro et al., 2001; Visser et al., 2003).

Derogatis and Derogatis (1990) view the psychosocial adjustment concept as one made up of intrapsychic processes, interactions between the person and other persons, as well as interactions taking place between the person and their sociocultural environment. These interactions are achieved by the roles he or she performs. Derogatis and Derogatis believe that it is the efficiency of these roles that highly correlate with the person's interpretation of their psychosocial adjustment.

Psychosocial adjustment is made up of many domains. The prominent domains included in the term are those that are, or are related to, people's significant role behaviours. Derogatis & Derogatis (1990) acknowledge that the person alone determines which domains are the most important in one's life. To create an objective measure, the authors undertook a combination of rational-deductive and empirical-analytic procedures,

which identified seven principal domains proving to be highly relevant to adjustment to illness. These domains include: Health Care Orientation (8-items), which addresses the person's attitudes and expectancies about the illness and treatment; Vocational Environment (6-items), which reflects the impact of the illness upon the person's work, school and/or home; Domestic Environment (8-items), which assesses problems in adaptation as experienced by the patient and family; Sexual Relationships (6-items), which measures any illness-related changes in the quality of sexual functioning or relationship; Extended Family Relationships (5-items), that measures any relational disruptions in the extended family constellation; Social Environment (6-items), reflecting the degree of impairment or constriction of the person's social and leisure activities; and Psychological Distress (7-items), which measures any distressing thoughts or feelings that the person may have in relation to the illness (Derogatis & Derogatis, 1990). These domains are used within the Psychosocial Adjustment to Illness Scale, which attempts to operationally measure a person's psychosocial adjustment to a chronic illness.

Based on Derogatis' seminal work within the area of psychosocial research, the remaining portions of this literature review will focus on research that has used the definitions and Psychosocial Adjustment to Illness Scale developed by Derogatis in respect to people diagnosed with cancer, specifically colorectal cancer. A description of the Psychosocial Adjustment to Illness Scale follows.

*An operational definition of psychosocial adjustment*

The Psychosocial Adjustment to Illness Scale (PAIS) was originally developed to take place in a semi-structured interview. Due to this costly and inconvenient method, the Psychosocial Adjustment to Illness Scale – Self Report Version (PAIS-SR) was developed. The tool is comprised of 46 items and refers the participant to “the past 30

days including today” (Derogatis, 1986). The questions are designed to assess the characteristics of a person’s adjustment in each of the seven previously described domains of the tool. Although each subscale measures the degree of adjustment to one’s condition within the specific domain, it is not correlated with the others, but is largely correlated with the total adjustment score (Derogatis & Fleming, 1996). Each item corresponds to a four-point scale with higher ratings indicative of poorer adjustment (Derogatis & Fleming, 1996). Scores can be obtained for adjustment in each of the seven domains and/or for overall adjustment as determined by the total of all the sub-scales.

Derogatis and Derogatis (1990) have outlined the method of scoring the PAIS-SR score and sub-scores. The PAIS-SR is scored by summing each of the seven domains and converting them to standardized area T-scores. This is done by referring the raw scores to a table of published norms. These standardized T-scores for the seven domains are summed to generate the PAIS Total Score. Summation of domain T-scores was chosen over raw scores to provide equal weighting of each domain in constructing the PAIS Total Score. Derogatis and Derogatis (1990) suggest that “respondents with a PAIS Total Score equivalent or greater than a T-score of 62 are positive for clinical levels of maladjustment” (p. 33).

Derogatis (1986) summarized the reliability of his instrument from three of his own research involvements. One of the samples involved a group of 89 people diagnosed with lung cancer, about whom demographics are not readily available in the academic literature. Although the overall coefficient for the scale is not stated, 5 of the 7 subscales have a coefficient greater than .80, and all of the scales range between .12 and .93 (Derogatis, 1986; Derogatis & Fleming, 1996). Both Derogatis and Derogatis and Fleming comment that the Extended Family subscale, with a coefficient of .12, has been



revised with the addition of a new item as well as other revisions. No comments are made about the internal consistency of that new subscale.

In her dissertation research exploring the relationships between psychosocial adjustment, social support and quality of life in adult colorectal cancer patients, Kelman (1995) addressed the psychometric properties of the PAIS-SR as part of her sub-analysis. She found an alpha reliability of .81 for the entire sample and .84 and .78 for men and women respectively.

Merluzzi & Martinez Sanchez (1997) conducted a principal axis factor analysis of the PAIS-SR in a sample of 502 adults with numerous types of cancer. This sample was predominantly people with breast cancer (47%), with colorectal cancer comprising 8% of the sample. The majority (72%) of participants in this study received chemotherapy as part of their treatment, and 49% of the subjects were diagnosed less than a year prior to entrance in the study. The entire PAIS-SR resulted with a coefficient alpha of .93, with the original subscales ranging from .50 to .87, five of which were over .80. The scales derived from the factor analysis yielded slightly higher coefficients.

Merluzzi and Martinez Sanchez (1997) report on the highly overlapping factor structure with the original scales of the PAIS-SR. In fact, correlations between the seven original scales and the seven-factor solution ranged from .82 - .99, with four of the scales correlating higher than .90, and one being unreported by the authors (Merluzzi & Martinez Sanchez, 1997). Their study also showed correlations of the subscales with other measures of adjustment to illness, disease impact and coping, which further supports the validity of the PAIS-SR for use in cancer research.

### *The cancer diagnosis and psychosocial adjustment*

Only a small number of studies have been conducted to explore the impact of psychosocial distress upon cancer patients. Both Derogatis and Derogatis (1990) and Wolberg et al. (1989) have illustrated that the cancer diagnosis alone contributes to a statistically significant poorer adjustment, in comparison to those who screen negative for a cancer diagnosis. Studies reviewing the magnitude of psychosocial adjustment in cancer patients have found that 20-30% of heterogeneous cancer patients (Greer, 1994; Harrison & Maguire, 1994), and as many as 38% of women diagnosed with breast cancer (de Paula Lima, 2005) experience moderate to high levels of psychosocial maladjustment. Therefore, just being given a cancer diagnosis affects a person's psychosocial adjustment, irrespective of treatments or symptoms.

### *Local cancer treatments and psychosocial adjustment*

Herranz and Gavilán (1999) attempted to determine the impact that two types of surgery had upon the laryngeal cancer patient's psychosocial adjustment. Patients either had radical surgery, in which all or nearly all of the larynx was removed, or functional surgery, which was more conservative and preserved laryngeal function. In determining the impact of radical or functional surgery upon the laryngeal cancer patient's psychosocial adjustment, Herranz and Gavilán (1999) found statistically non-significant differences between the groups. However, when comparing the global T scores for these surgical groups, the radical group (56.92) showed slightly worse adjustment than the functional group (56.44), in comparison to the reference cancer patient's group, whose global T score was 50. Similarly, in her study comparing women with breast cancer who had breast-conserving surgery or mastectomy, Hoskins (1997) found non-significant differences between the groups on the Psychological Distress scale of the PAIS at three

assessments during the first year after surgery. The mean of the Psychological Distress scale for the entire sample, regardless of surgery, was found to be moderate at 13.10 (possible range = 0-28, alpha 0.89). However, both treatment groups' psychological distress scores significantly improved over the course of the year. Residual disturbances in psychosocial adjustment were found by Wolberg et al. (1989) in women up to 16-months after having breast cancer surgery. Collectively, these studies could indicate that cancer surgery, regardless of how extensive or disfiguring, comparatively affect the cancer patient. The magnitude that these treatments have upon the cancer patient's psychosocial adjustment is moderate and is likely to improve over an uncertain period.

Psychosocial adjustment has also been explored in relation to radiation therapy as a treatment for cancer. Hassey Dow & Lafferty (2000) assessed the pre- and post-treatment psychosocial adjustment scores for women receiving radiation treatment for early-stage breast cancer. Again, only moderate scores of psychosocial maladjustment were found in this sample, but a statistically significant improvement in psychosocial adjustment scores were found to occur in the time between beginning and ending treatment, showing that localized cancer treatments are comparable in how they affect the cancer patient's psychosocial adjustment.

#### *Systemic cancer treatments and psychosocial adjustment*

Hoskins' (1997) comparison of the Psychological Distress subscale of the PAIS-SR in breast cancer patients receiving either chemotherapy or not, failed to find a statistically significant difference between these groups at either one or two months post-treatment initiation (at a comparable time point for the non-chemotherapy group). However, a significant difference was found at 3-months, and again at six months after treatment initiation. Hoskins' (1997) study clearly shows the differences between cancer

patients receiving systemic treatment or not and suggest that adjustment is a process occurring over time.

Another study addressing chemotherapy and adjustment found significantly poorer adjustment on five of the seven PAIS domains in a group of patients who withdrew from chemotherapy treatment in comparison to those who completed standard treatment (Gilbar & De-Nour, 1989). The reasons that patients refused to continue on their treatment are not clear within the article outlining the study. However, Gilbar and De-Nour (1989) do highlight that neither group's scores were high enough to be a sign of psychosocial maladjustment, as indicated by the tool developer. This finding contradicts that previously presented by Hoskins (1997) thus necessitating further research into relationships between chemotherapy treatments and psychosocial adjustment.

#### *Potential confounders to psychosocial adjustment in cancer patients*

Factors other than a cancer diagnosis or treatment may also affect the cancer patient's psychosocial adjustment. In her study exploring the factors contributing to adjustment and quality of life in women diagnosed with cancer, Noukki (2000) outlined the strongest predictors of poorer psychosocial adjustment. These included having less social support, attributing the cause of the illness to bad-luck or self blame, holding back on what one wants to do as a result of the illness, attributing control over the illness to chance and finding less positive meaning out of the illness experience. While the characteristics of disease treatment are not known to the reader, time since diagnosis was a major variable within the analyses.

#### *Psychosocial adjustment and colorectal cancer*

Most of the studies assessing psychosocial adjustment in colorectal cancer patients, have compared the adjustment scales of those who did to those who did not have

stoma-related surgery. Although Canadian statistics on the incidence of colorectal cancer related stomas are unknown, the American Cancer Society estimates that 1 in 8 Americans diagnosed with rectal cancer require a permanent colostomy as part of their cancer treatment (2005). Compared to non-stoma bowel surgeries, stomal surgery in a combined sample of malignant and benign colorectal diseases appears to increase the incidence of psychosocial difficulties during the first four post-operative months (Bekkers, van Knippenberg, van den Borne, & van Berge Henegouwen, 1996). Specifically related to those who have a colostomy related to colorectal cancer, Kelman (1997) found that 10% of women and 7% of men have been found to have positive clinical levels of psychosocial maladjustment one year after diagnosis.

Nishigaki and colleagues (2007) sought to explore the influence of life stage, seniors (aged > 65 years) to non-seniors (age < 65 years), upon the psychosocial adjustment of colorectal cancer patients without stomas ( $n = 93$ ). They used the Japanese version of the Psychosocial Adjustment to Illness Scale – Self Report, which uses 6 of the 7 domains of the original PAIS-SR, omitting the Health Care Orientation subscale. It is not clear as to why these tools vary. Nishigaki's team (2007) conducted a multiple regression analysis, treating each subscale of the PAIS-SR as a dependent variable and background factors, such as years of education, marital status and occupation, as explanatory variables. They found that Psychological Distress was the only domain that differed between the two life stages, with seniors exhibiting less psychological distress than the non-seniors ( $44.7 \pm 7.7$  and  $48.6 \pm 9.4$ , mean and standard deviation respectively). The other five domains did not differ significantly between the groups and total PAIS-SR scores were not analyzed as the entire original version was not used. This

analysis outlined differences between the two life stages for each of the PAIS-SR subscales.

In their study of colon cancer patients' adjustment scores during the first year after surgery, Northouse, Mood, Templin, Mellon, and George (2000) found that men and women follow a similar trend: low at diagnosis, reaching the highest point at two months, and then declining to near-baseline scores at one-year, although women had slightly lower scores than baseline. Alternatively stated, patients experienced more problems with adjustment during their chemotherapy treatments before improving to near baseline levels. In looking at the measures of adjustment, Northouse and colleagues (2000) found significant correlations among the PAIS scores at all three time points: between baseline and 2-months, baseline and 1 year, and 2 months and 1 year. Both of these studies illustrate the general trend of psychosocial adjustment in colorectal cancer patients during the first year after diagnosis and surgery, indicating the importance of psychosocial care received from their health care practitioners.

Nishogaki (2007) also explored the period since diagnosis in relation to the PAIS-SR subscales. The duration since diagnosis significantly contributed to the seniors' maladjustment in the Social Environment Domain only. Whereas, only the Vocational Environment Domain was significantly impaired by the time since diagnosis in the non-seniors group. Collectively, these studies illustrate that there are disturbances in the psychosocial adjustment of colorectal cancer patients that vary over time and are related to situation and background factors. This indicates the importance of the health care team in monitoring a cancer patient's psychosocial adjustment and its components.

### *Psychosocial adjustment and cancer outcomes*

Few studies have addressed the impact of psychosocial interventions on disease outcomes of people diagnosed with cancer. In a review of the literature, Walker, Heys, and Eremin (1999) comment on the accumulating evidence that psychosocial interventions play in improving cancer patients' quality of life and prolonging their survival. Outside of their review is a randomized controlled trial identifying the impact that counseling and support interventions have upon patients' psychosocial adjustment. Cain, Kohorn, Quinlan, Latimer, and Schwartz (1986) randomized women recently diagnosed with gynecological cancer to receive individual counseling, group counseling or standard care. Using the PAIS to measure psychosocial adjustment, Cain and her colleagues found no significant differences in the women's baseline results, but found that women who completed the individual or group counseling had significantly improved adjustment 6 months after the intervention.

In terms of cancer survival, Goodwin et al. (2004) found no association between early-stage breast cancer patients' overall medical outcome and their psychosocial status at either diagnosis or 1-year. Although the study of psychosocial interventions' outcomes are minimal, and show statistically weak and varying results, practitioners should be cognizant of the impact that attention to psychosocial needs has upon their patients' overall satisfaction with the professional care they receive (Walker et al., 2003).

### *Quality of Life*

#### *Toward a definition of quality of life, as related to the oncology literature*

Through the 1970s, as cancer treatments began to become more successful and patients were living longer after a cancer diagnosis, more attention was directed toward quality of life. A clear definition of quality of life remains elusive, however, it is

generally agreed that it is a subjective, unique, multi-dimensional concept (Giesler, 2000).

In an attempt to define the concept of quality of life in relation to oncology, Cella and Tulsky (1993) acknowledged the centrality of subjectivity in determining one's quality of life. They proposed that quality of life be defined as "patients' appraisal of and satisfaction with their current level of functioning compared to what they perceive to be possible or ideal" (Cella & Tulsky, 1993).

Factor analyses and scale aggregation studies (Cella, 1992) have supported the validity of four primary dimensions of quality of life: physical, functional, emotional and social. The physical dimension refers to the person's perceived and observed bodily function as related to disease symptoms or treatment side effects. Functional well-being refers to the person's ability to perform activities of daily living, and actions that meet one's ambitions and social roles. A person's emotional well-being is related but distinct from their physical well-being and may reflect a positive or negative affect. Lastly, the social dimension includes one's perceived social support, maintenance of leisure activities and family functioning. These dimensions serve to guide the measurement of quality of life from the patient's perspective as it is important to assess one's needs, evaluate treatment outcomes and predict responses to further treatment (Cella, 1992).

#### *Measurement of quality of life in the oncology literature*

A number of tools have been developed to measure quality of life, but two are predominant within the oncology literature: the European Organization for Research and Treatment of Cancer (EORTC) QLQ-C30 and the Functional Assessment of Cancer Therapy – General Scale (FACT-G) (Holzner et al., 2006).

The EORTC QLQ-30 is a 30-item questionnaire made up of multi-item scales and single items that reflect what the EORTC unclearly defines as a multi-dimensional quality



of life (Aaronson et al., 1993). The nine multi-item scales include five functional scales (physical, role, cognitive, emotional and social), three symptom scales (fatigue, pain and nausea and vomiting), and a global health and quality of life scale. The remaining single item questions address issues common among cancer patients such as dyspnea, loss of appetite, sleep disturbance, diarrhea, constipation and disease/treatment financial impacts. The tool has been found to be reliable and valid (Aaronson et al., 1993).

The FACT-G arose from an attempt to develop a brief, valid and reliable tool to measure general quality of life in patients receiving cancer treatment. Cella, Tulsky, Gray and colleagues (1993) undertook a five-phase validation process involving 854 patients with cancer and 15 oncology specialists. After an initial pool of patients and professionals completed an open-ended interview, items were overlapped and then further reduced to compile a version containing 38 items. After factor and scaling analyses of this initial version with a large population of patients with mixed cancer diagnoses, a final version of the FACT-G was developed. The result, a 27-item highly reliable, valid and sensitive tool, available in numerous languages, and has been widely used in heterogeneous cancer populations in an array of research studies and clinical trials.

In 2006, Holzner and colleagues sought out to equate the EORTC QLQ-C30 and FACT-G using classical test theory and the Rasch measurement model. In addition to collecting sociodemographic data, each of the measures were given to a sample of heterogeneous cancer patients ( $n=737$ ), 362 (49%) who completed the EORTC-QLQ-C30 first and 375 (51%) who completed the FACT-G first. The data analysis showed that three of the tools' domains were equatable: the physical, emotional, and functional/role domains. Discrepancies were found for the social domains of the tools. As such,

conversion tables were constructed for the 3 domains that were comparable which will be useful for future quality of life meta-analyses, translations and interpretations.

*Functional Assessment to Cancer Therapy – General (FACT-G)*

It is the FACT-G that will be used to further explore quality of life in the cancer related literature. The core questionnaire (Version 4) assesses 4 domains and employs Likert-type questions ranging from 0 ('not at all') to 4 ('very much'). The domains and ranges of scores for each are as follows: Physical Well-Being (PWB) (7-items, range 0-28), Social/Family Well-Being (SFWB) (7-items, range 0-28), Emotional Well-Being (EWB) (6-items, range 0-24) and Functional Well-Being (FWB) (7-items, range 0-28) (Cella, Hahn, & Dineen, 2002). The total FACT-G score is the sum of the four subscales (range 0-108), and is computed if greater than 80% of the items have a response (Brucker, Yost, Cashy, Webster, & Cella, 2005). Higher overall scores are associated with increased satisfaction with quality of life. Normative data for general and cancer patient populations are available (Brucker et al., 2005).

*Quality of life, cancer, and treatment-related side-effects*

Quality of life has been studied in relation to cancer diagnoses, treatments and side-effects. Studies of heterogeneous groups of cancer patients have found that disease symptoms and psychological variables have explained as much as 44% of the variance of quality of life. For example, in their prospective study determining the rates and course of emotional distress, cognitive function and quality of life in cancer patients treated with chemotherapy, Iconomou et al. (2004) found that at the end of treatment, depression was the sole predictor of quality of life, explaining 44% of the variance. Similarly, Redeker et al., (2000) found through a hierarchical regression analysis, that depression and anxiety explained 43% of the variance in quality of life. Other disease and treatment side-effects

that have been negatively correlated with quality of life include gender, fatigue, menopausal symptoms induced by chemotherapy, receiving current treatment, insomnia, depression and anxiety (Parker, Baile, De Moor, & Cohen, 2003; Redeker et al., 2000; Tchen et al., 2003).

### *Quality of life, cancer stage and treatment*

Measures of quality of life have not been found to be associated with medical outcomes, specifically for women with early-stage breast cancer (Goodwin et al., 2004). In fact, studies of quality of life in relation to cancer treatment have found an initial decrease in overall quality of life within the first few months after diagnosis (Visser et al., 2003; Hassey Dow & Lafferty, 2000), while longitudinal studies find these levels return to baseline levels within 6 months after treatment is completed (Hassey Dow & Lafferty, 2000). More discriminating studies have found that the type of treatment administered, specifically chemotherapy, significantly impacted the cancer patient's quality of life as compared to other cancer treatments (Ahles et al., 2005; Jenkins et al., 2006).

The literature has shown varying results when looking at quality of life (FACT-G) in relation to the stage of cancer. Specifically related to chemotherapy treatments, Iconomou et al. (2004) found that patients scheduled to receive first-line metastatic chemotherapy reported a significantly poorer quality of life compared to those commencing adjuvant chemotherapy.

Although destined to determine age-related differences in quality of life in cancer patients, the sample collected by Mkanta, Chumbler, Richardson, & Kobb (2007) was largely comprised of late-stage (2/3) cancer patients (91%) undergoing 6-months of chemotherapy. They found that tumour stage and performance status were not significantly related to quality of life. In fact, among the older adults (> 65 years), the

unadjusted mean of the overall quality of life score was found to increase over the 6-month treatment period.

In their study documenting quality of life, symptom distress and performance status, Hwang, Chang, Fairclough, Cogswell, & Kasimis (2003) assessed 67 advanced cancer patients at 3-6 week intervals from the time of no active anti-cancer treatment to their death. They found that overall quality of life scores steadily deteriorated from 6 months prior to death, with a rapid decline occurring in the final 2-3 months prior to death. Correlations between performance status and overall quality of life were significantly correlated at 2 to 6 months before death, but no such correlation was found in the last 2 months of life with any of the quality of life sub-scales.

Although these studies indicated opposing results for the quality of life in advanced cancer patients, the differences may be attributed to treatment and imminent disease prognosis.

#### *Quality of life and colorectal cancer*

Studies have been done to investigate issues related to quality of life from the perspective of the patient living with colorectal cancer. Although some issues related to the colorectal cancer patient's quality of life appear to be similar to the larger, heterogeneous cancer population, these patients do have some quality of life issues that are unique to them and have resulted in poorer overall quality of life scores (Mkanta et al., 2007). These factors include pain, constipation, fatigue, diarrhea and non-cancer chronic health problems (Arndt, Merx, Stegmaier, Ziegler, & Brenner, 2004; Cameron, 2005; Esnaola et al., 2002; Rauch, Miny, Conroy, Neyton, & Guillemin, 2004; Trentham-Dietz et al., 2003).

In their randomized study assessing the relationship between the type of colorectal surgery and quality of life, Weeks, Nelson, Gelber, Sargent, and Schroeder (2002) found that for up to two months post-operatively, quality of life was unrelated to whether patients had undergone laparoscopic surgery or an open colectomy. Alternatively, a systemic review within the Cochrane Database claimed that varying study findings made it impossible to make firm conclusions relating stoma-producing surgery with quality of life (Pachlar & Wille-Jorgensen, 2005).

In her longitudinal, cohort study, Vardy (2007) noted that 23% of patients had a decline in overall quality of life from pre- to post-chemotherapy assessments, whereas there were no declines seen in the control group for this time period. These findings failed to reach statistical significance.

These findings collectively illustrate the need for further studies assessing the quality of life from the perspectives of patients living with colorectal cancer.

#### *Cognitive Dysfunction, Psychosocial Adjustment and Quality of Life*

As outlined in the previous sections, cognitive function related to cancer and its treatments have been understudied, while quality of life related to cancer and its treatments has received a significant amount of attention in the academic literature. There is also very little research relating the cognitive dysfunction that cancer patients experience to their quality of life. Iconomou et al. (2004) explored the relationship between cognitive performance, as determined by the Mini-Mental State Examination (MMSE), and global quality of life, as determined by the European Organization for Research and Treatment of Cancer (EORTC) QLQ-C30, in a group of heterogeneous cancer patients completing chemotherapy. They found that the participants' scores on the MMSE had a small, negative, although non-significant, correlation with global quality of

life. However, when exploring the participants' perception of their cognitive dysfunction, as determined by the Cognitive Subscale of the EORTC-QLQ30, the researchers found a statistically significant positive correlation with global quality of life. From this study, it is clear that quality of life is impacted by one's perception of a poorer cognitive function rather than by an actual impairment in function. Similar studies of women receiving chemotherapy for breast cancer have also found no statistical association between objective cognitive function scores and quality of life (Tchen et al., 2003; Brezden et al., 2000), but acknowledge the small incidence of cognitive dysfunction resulting from chemotherapy results in a small sample size having insufficient power to make definitive conclusions (Tchen et al.).

In their review of the literature, Desai, Butt, Sabatino, and Wagner (2005) acknowledge that although cognitive dysfunction has been demonstrated in cancer patients receiving chemotherapy through neuropsychological and patient self-report, there have not been validated instruments to assess self-reported cognitive dysfunction. The authors decided to address this gap by developing and validating a cancer-specific self-report tool to assess cognitive impairments and the impact of these impairments on the patient's quality of life. Using information gathered from interview and focus groups in which patients said that cognitive impairments impacted their quality of life and functional status, a thematic content analysis resulted in a Functional Assessment of Cancer Therapy-Cognitive subscale (FACT-Cog). Further studies using the FACT-Cog have found it to be a reliable and valid tool which has demonstrated higher internal consistency reliability and convergent validity than other comparable tools within oncology research (Jacobs, Jacobsen, Booth-Jones, & Wagner, 2004). Collectively these

studies show the increasing recognition of the relationship between cognitive function and quality of life in cancer patients.

### *Psychosocial Adjustment and Quality of Life*

In using the previously mentioned definition of psychosocial adjustment developed by Derogatis and Derogatis (1990), very little has been found within the scholarly literature to relate the concepts of psychosocial adjustment and quality of life. In a longitudinal study examining quality of life and psychosocial adjustment in breast cancer patients receiving radiation, results fail to show any significant differences in psychosocial adjustment or quality of life from the beginning to conclusion of treatment therapy (Hassey Dow & Lafferty, 2000). Although the two concepts were not examined for correlations with each other, the trend in their overall scores failed to show significant differences between the two concepts at the same time points of the disease/treatment trajectory. In his case-control, quasi-experimental study, Batton (2000) found a statistically significant correlation between pre-test and post-test scores of the PAIS and quality of life in a group of heterogeneous cancer patients. Specifically related to colorectal cancer patients, Kelman's (1997) study of the relationships between psychosocial adjustment and quality of life found a significant relationship for the total sample, as well as between men and women. These studies concur about this inverse relationship indicating that those who report fewer problems with adjustment report a higher quality of life. In further relating these concepts, Kelman (1997) used a multiple regression analysis to find that approximately 18% of the variance in quality of life was accounted for by psychosocial adjustment in the total sample, and 23% and 19% for men and women respectively. These results illustrate the relationship between quality of life

and psychosocial adjustment indicating that those who report fewer adjustment problems report a higher quality of life.

### *Summary of the literature*

In summary, there is insufficient exploration relating psychosocial adjustment as defined by Derogatis and Derogatis (1990) to quality of life (as defined using the FACT-G), although the concepts have been thoroughly studied individually. There is a paucity of research that has related cognitive dysfunction to quality of life, and even less that has explored how cognitive dysfunction impacts the cancer patient's psychosocial adjustment. Therefore, the purposes of this research are: (a) to clarify the relationship between the concepts of psychosocial adjustment and quality of life, and (b) to gain further understanding of how chemotherapy-induced cognitive dysfunction impacts these concepts in relation to the experience of living with colorectal cancer.

### *Research Questions*

1. What impact does adjuvant chemotherapy-induced cognitive dysfunction have upon the colorectal cancer patient's psychosocial adjustment?
2. Does psychosocial adjustment differ between people diagnosed with colorectal cancer who do and do not receive adjuvant chemotherapy?
3. What is the relationship between psychosocial adjustment and quality of life within a sample of colorectal cancer patients?

## Chapter III

### *Methodology*

#### *Study Design*

A descriptive, correlational design was used to explore the relationships between cognitive dysfunction and psychosocial adjustment, as well as psychosocial adjustment



and quality of life in adults diagnosed with non-metastatic colorectal cancer. The sample was recruited from a larger, prospective, longitudinal cohort study of cognitive function, fatigue and quality of life in patients with localized colorectal cancer.

### *Study Population*

Patients with histologically confirmed stage A, B or C colorectal cancer, who had undergone surgical resection, were eligible to participate in this study. The sample consisted of 4 groups: Groups A & C (stage III/ high-risk II disease), with Group A assessed pre-chemotherapy and Group C post-chemotherapy; while Groups B & D (stage I/II disease) included those that did not require chemotherapy, with Group B assessed post-operatively and Group D assessed 6-months post-operatively.

All participants were 18-75 years of age; had an ECOG performance score of 0 (fully active, able to carry on all pre-disease performance without restriction) or 1 (restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature) (Eastern Oncology Cooperative Group, n.d.); had a life expectancy of at least 12 months; and had adequate hepatic function documented by a serum bilirubin < 18  $\mu\text{mol/L}$  and liver function tests within 1.5 times normal range.

The criteria for the study excluded those with any major pre-existing psychiatric history or dementia, alcohol abuse, or those using psychotropic medication that might lead to cognitive problems, other than short acting benzodiazepines for nausea or sleep. Patients with a pre-existing neurological condition that was likely to interfere with their ability to perform cognitive testing were also excluded. Other exclusion criteria included evidence of metastatic disease; ongoing sepsis, or uncontrolled or HIV infection; other severe co-morbidity making participation inappropriate to this study; active cancer within the past 5 years; previous history of chemotherapy; and minimal English skills such that

subjects would not be able to follow simple written English instructions and to read questionnaires of a grade 8 standard with the help of a research assistant.

The study was initiated with participants being recruited from eight hospitals in Toronto. Due to difficulties in obtaining the projected sample size, permission was granted to expand the study into two hospitals in Sydney, Australia, where the larger study was in operation. This action was deemed acceptable due to the similarities in demographic of these countries. Each institution's Research Ethics Board approved the study, and all participants gave written informed consent.

### *Sample Size*

A moderately strong association between the variables of interest was defined as present if the Pearson correlation coefficient was 0.35 or higher (this is equivalently found when using a linear regression model with only one predictor variable). To test the null hypothesis ( $H_0: r = 0$ ) versus the alternative hypothesis ( $H_A: r = 0.35$ ), with an  $\alpha = 0.05$  and 80% power, a total sample size of 64 patients was required. Thus, the aim was to accrue 16 patients to each of the four treatment groups, which gave sufficient power to detect moderately strong associations. It was determined that if the relationship between cognitive ability and psychosocial adjustment were different between the groups, then the association would be estimated for each treatment group individually. In this situation, sufficient power was still present to detect a strong relationship ( $\alpha = 0.05$ , power = 80% to detect a correlation of 0.64).

### *Data Collection Procedures*

In the larger prospective, longitudinal study, participants completed a series of assessments in the following order: traditional neuropsychological tests; four batteries from the Cambridge Neuropsychological Test Automated Battery (CANTAB); the

Functional Assessment of Cancer Therapy – Cognition (FACT-Cog); the Functional Assessment of Cancer Therapy – General (FACT-G); the Functional Assessment of Cancer Therapy – Fatigue (FACT-F); the General Health Questionnaire (GHQ); and a series of laboratory tests. These assessments were conducted at baseline (either prior to chemotherapy administration for the cases, or within 12 weeks of surgery for the control group), and afterward at 6, 12 and 24 months.

For the purposes of this smaller correlational study, subjects were approached for participation at their baseline and 6-month assessment within the larger study (refer to Appendix A for the study schemata). At only one of these assessments were the subjects approached by the researcher to discuss this study's objectives and requirements. If subjects were agreeable, they were given a package containing an Informed Consent Form, the Psychosocial Adjustment to Illness Scale – Self Report Version (PAIS-SR) and a return addressed, stamped envelope in which the completed consent form and PAIS-SR was returned to the researcher. If a package was not returned within two weeks, the researcher made a courtesy reminder call to the patient. A log was kept of each distributed package for recruitment statistics.

The consent forms for this study identified that the CANTAB and questionnaire scores would be retrieved from the larger study, should patients agree to participate in this research. Therefore, by signing the consent form to participate in this study, participants were agreeing to this retrieval.

#### *Measurement Tools and Operational Definitions*

##### *Cambridge Neuropsychological Test Automated Battery (CANTAB)*

The CANTAB has been assessed for both reliability and validity. Of concern in longitudinal studies exploring cognitive function is the test/re-test reliability, which the

CANTAB has been shown to be highly acceptable ( $r = 0.75-0.80$ ) (Lowe & Rabbitt, 1998). The tool has also been validated through a factor analysis with varimax rotation in a large sample of healthy individuals (Robbins et al., 1994). Together these results appreciate the use of the CANTAB within research on cognitive function.

Due to the previously mentioned time taken to complete the entire battery, four tests were selected to assess the most common domains assessed in cognitive function: the Motor Screening test (MOT), the Reaction Time test (RTI), the Rapid Visual Information Processing test (RVP), and the Spatial Working Memory test (SWM). For exploratory purposes, a Total Reaction Time (TRI) score was calculated using the MOT reaction time and the RVP reaction time. Also for exploratory purposes, a Problem Solving Speed Measures (PSSM) score was calculated using the Five Choice Movement and Reaction Times of the RTI, in addition to the SWM latency.

Z-scores were used to gauge cognitive performance within this study. The tests used from the CANTAB provided demographically corrected Z-scores for each test, with a higher score indicating better performance.

Also of interest, were Global Deficit Scores (GDS) that were used to define cognitive impairment. Cognitive impairment was defined by a GDS of  $\geq 0.5$ , which has been shown to provide an optimal balance between specificity (0.89) and sensitivity (0.39) (Carey et al., 2004). As stated in preceding sections, GDS's are commonly calculated using demographically corrected T-scores, whereas the CANTAB reports Z-scores for each test. Therefore, the CANTAB Z-scores were converted to T-scores using a table developed by Anderson (personal communication, October 10, 2008), which then allowed for GDS's to be determined. Anderson's conversion table is summarized in Table 2, along with the Deficit Scores as outlined by Carey et al. (2004).

Table 2: A Table Relating T-Scores and Z-Scores to Global Deficit Scores

T-Score	Z-Score	Deficit Score	Impairment Descriptor
$\geq 40$	$> 0.99$	0	Normal
39-35	- 1.0 – -1.49	1	Mild
34-30	- 1.5 – -1.99	2	Mild to Moderate
29-25	-2.0 – -2.49	3	Moderate
24-20	-2.5 – -2.99	4	Moderate to Severe
$\leq 19$	$\leq -3.0$	5	Severe

*Psychosocial Adjustment to Illness Scale – Self-Report Version (PAIS-SR)*

The PAIS-SR (Derogatis, 1990) is a useful tool for assessing subject's overall adjustment to illness, as well as their adjustment to a number of domains of psychosocial adjustment. The internal consistency reliability of the entire tool has been reported in a number of oncology studies ranging from a Cronbach's alpha of 0.93 in heterogeneous cancer samples (Merluzzi & Martinez Sanchez, 1997) to 0.81 in samples of people diagnosed with colorectal cancer (Kelman, 1997). Factor structure and correlations with disease impact, adjustment and coping, all support the validity of the PAIS-SR and its use within the oncology research (Derogatis & Fleming, 1996; Merluzzi & Martinez Sanchez, 1997).

Therefore, the PAIS-SR has both reliable and valid strengths for usage within oncology research and was used to measure the psychosocial adjustment in the current research study. Although the Total PAIS-SR score was the variable of interest, exploratory analyses individually investigated each of the seven domains of the tool.

Participants were asked to complete the 46 items representing the seven domains of the PAIS-SR. Each domain score was converted to a standardized area T-score and summed to generate a Total Score. A score of greater than or equal to 62 indicated maladjustment, as indicated by Derogatis and Derogatis (1990).

### *Functional Assessment of Cancer Therapy – General measure (FACT-G)*

As outlined in the preceding sections, the FACT-G has been widely used within cancer research. In studies of large, heterogeneous cancer samples, the FACT-G has shown a high internal consistency reliability ( $\alpha = 0.89$ ) (Cella, Tulsky, et al., 1993; Mkanta, et al, 2007) and high convergent validity ( $r = 0.79$ ) with other quality of life tools in the oncology literature (Cella, Tulsky, et al., 1993). For these reasons, the FACT-G was determined to be an appropriate tool to assess quality of life in this sample. Again, although the total FACT-G score was of primary interest, the four sub-scale scores were explored individually.

Participants were asked to complete the 27 items representing the 4 subscales of the FACT-G. The total FACT-G score, which is the sum of the scores for the four subscales, was used to quantify quality of life (Brucker et al., 2005). A higher FACT-G score indicates a higher quality of life.

### *Data Analysis*

Once the data were collected, each measure was scored according to the procedures identified by the developer. SAS version 9.1 was used for all statistical analyses. Statistical significance was defined as a p-value of 0.05 or less and all tests were two-tailed.

Descriptive statistics, such as the median, range, frequency and proportion were used to summarize patient characteristics and study assessments. Medians and ranges were the preferred methods of reporting due to the small numbers within treatment groups. It is well known that the impact of an outlying result is greater upon the mean of a small sample than that of a larger sample. For consistency, the medians and ranges of both the treatment groups and the collective sample is reported.

This cohort of patients was evaluated for comparability with the entire patient cohort in the larger study by visual comparison. Data used as a measure for the entire patient cohort were those used as part of a presentation at the American Society of Clinical Oncology's Annual Meeting 2008. Comparisons of questionnaires between groups were performed using the Kruskal-Wallis test for continuous outcomes and the  $\chi^2$ -test for binary outcomes. Scores which had statistically significant differences between groups, were further evaluated using pair-wise comparisons.

Linear regression methods were used to evaluate associations between psychosocial adjustment, cognitive function, quality of life and the effect of patient group on the associations. A regression model was constructed with psychosocial adjustment as the outcome variable (measured by the PAIS-SR Total T-Score), and cognitive function (measured by the CANTAB Z-score) as the predictor variable. The effect of patient group was evaluated by including a factor for group and an interaction between cognitive function and group. If neither the interaction variable nor the group factor was significant as a predictor then the original model with only cognitive function was used. A similar process was used to evaluate the association between psychosocial adjustment and quality of life (measured by FACT-G). Level of association was estimated using the Pearson's correlation coefficient and 95% confidence intervals calculated using Fisher's Z transformation including the bias adjustment.

There was no multiple testing adjustment of the p-value, as the expectation was that there would be only one primary outcome test (whether the association between cognitive ability and psychosocial adjustment was significant across all patients). All secondary evaluations were considered exploratory and p-values have been reported for these tests.

## Chapter IV

### *Results*

#### *Sample Characteristics*

Between February 1, 2006 and June 30, 2008, 110 patients were approached to participate in this study. Of those, four were excluded due to lack of informed consent, one was excluded due to metastatic disease, five were excluded due to having previously completed the PAIS-SR, and 26 did not return the study documents despite a courtesy reminder call. This resulted in a sample size of 74 non-metastatic colorectal cancer patients participating in this study.

It is important to note that five subjects were tested twice each. These participants were approached during a time when study recruitment appeared to be slowing. The analysis was re-run using only one evaluation per patient and using methods which incorporate an assumed correlation for these subjects (i.e. generalized estimating equations). Results were similar in all cases. Therefore, the analysis includes all available data, including the participants who completed assessments twice, in attempt increase the study's power.

Baseline demographic characteristics are presented in Table 3. This patient sample was similar in age (median=61.0, range 23-75) and gender (39% female) as compared with the patient demographics of the larger study (median age=58, range 23-75, 38% female).



Table 3: Sample Characteristics

Characteristic	N	Percentage
Gender		
Male	45	60.8
Female	29	39.2
Marital Status		
Married/Common-Law	51	75.0
Separated/Divorced	6	8.8
Single	10	14.7
Widowed	1	1.5
Highest Level of Education Achieved		
Secondary	18	26.9
College/University	35	52.2
Post-Graduate	14	20.9
Alcohol Use (No. of drinks/day)		
0	30	47.6
1	26	41.3
2+	7	11.1
Smoking Status		
No	40	54.8
Yes	3	4.1
Ex	25	34.3
Psychiatric Drugs		
No	55	90.2
Yes	6	9.8
Age	74	61.0 (23.6-75.9) <i>Median (range)</i>

The majority of the sample were married or common-law, over half of the sample had completed college or university, most drank none or little alcohol, and most were non-smokers.

Table 4 outlines the disease stage and treatments for the study sample. The majority of the case groups had had surgery where full staging was assessed. Four of the cases were receiving neo-adjuvant chemotherapy prior to surgery so full staging was not able to be determined at the time of the study assessment. For another 21 study

participants, their staging was undetermined. Since cancer stage was collected for exploratory purposes only, these data were captured as “missing”.

Table 4: Sample Treatment Characteristics

Characteristic	N	Percentage
<b>Cancer Stage</b>		
A	18	25.7
B	15	21.4
C	12	17.1
Neo-Adjuvant	4	5.7
Missing	21	30.0
<b>Group</b>		
A (Pre-Chemo)	19	25.7
B (Post-Surgery Control)	18	24.3
C (Post-Chemo)	20	27.0
D (6-month Post-Surgery Control)	17	22.9
<b>Chemotherapy Type (Groups A &amp; C only)</b>		
5 Fluorouracil	1	3
5 Fluorouracil + Oxaliplatin	17	46
Capecitabine	2	5
Capecitabine + Oxaliplatin	1	3
5 Fluorouracil + Radiation	12	32
Missing	4	11

### *Cognitive Function*

As expected, the CANTAB deficits seen in this group of patients were similar to the larger study (25.0% vs. 22.0-29.0% respectively). No significant differences were seen between the groups for either the CANTAB score or any of it's individual tests.

These results are displayed in Table 5.

Table 5: Median (ranges) of CANTAB and Test Scores

	Total Sample	Group A (Pre-Chemo)	Group B (Post-Surgery Control)	Group C (Post-Chemo)	Group D (6-Months Post-Surgery Control)	p-value <sup>4</sup>
N	64	16	13	20	15	
CANTAB Z-Score	-0.8 (-11.0, 6.2)	-0.2 (-6.3, 4.4)	-1.4 (-11.0, 4.7)	-0.4 (-6.4, 5.2)	-0.8 (-7.3, 6.2)	0.94
MOT <sup>1</sup> Z-Score	0.2 (-2.9, 0.9)	0.1 (-0.8, 0.9)	-0.1 (-2.9, 0.8)	0.3 (-1.0, 0.8)	0.2 (-1.4, 0.8)	0.50
RTI <sup>1</sup> Z-Score	-0.1 (-5.4, 2.7)	-0.3 (-5.4, 2.3)	-0.4 (-2.6, 2.1)	0.1 (-3.3, 1.9)	-0.0 (-5.0, 2.7)	0.72
RVP <sup>1</sup> Z-Score	0.2 (-3.3, 3.1)	0.2 (-1.7, 3.1)	0.1 (-3.0, 2.3)	-0.3 (-3.3, 2.8)	0.4 (-2.0, 2.6)	0.64
SWM <sup>1</sup> Z-Score	-0.6 (-3.1, 3.5)	0.3 (-3.0, 2.8)	-0.7 (-3.1, 2.9)	-0.5 (-2.7, 3.5)	-0.7 (-2.5, 2.4)	0.89
TRI <sup>2</sup> Z-Score	0.1 (-5.9, 3.1)	0.2 (-1.9, 2.9)	-0.4 (-5.9, 3.1)	0.0 (-3.5, 3.0)	0.5 (-1.8, 3.1)	0.61
PSSM <sup>3</sup> Z-Score	-0.5 (-5.8, 5.0)	-0.7 (-5.3, 2.5)	-0.5 (-5.1, 3.2)	-0.3 (-5.6, 5.0)	-0.4 (-5.8, 4.2)	0.80
CANTAB Deficits N (%)	16 (25.0)	6/16 (37.5)	1/13 (7.7)	4/20 (20.0)	5/15 (33.3)	0.25

<sup>1</sup> = Tests within the CANTAB: Motor Screening test (MOT); the Reaction Time test (RTI); the Rapid Visual Information Processing test (RVP); and the Spatial Working Memory test (SWM).

<sup>2</sup> = Total Reaction Time (TRI) computed using the MOT and RVP reaction times.

<sup>3</sup> = Problem Solving Speed Measures (PSSM) computed using the RTI's Five Choice Movement and Reaction Times as well as SWM latency.

<sup>4</sup> = Applies only to the pair-wise comparisons of Groups A thru D. Does not include Total Sample results.

### *Psychosocial Adjustment*

The Kruskal-Wallis test was used to explore differences between groups for the PAIS-SR and it's subscales. These results are reported in Table 6. Significant differences were found between groups, specifically the 6-month post-surgical control, in terms of PAIS Total T-score (p=0.049). There was also a statistically significant difference found for the Total T score when comparing the 6-months post-surgery control

group and the post-chemo group ( $p=0.008$ ), with the 6-months post-surgical control showing better adjustment.

When exploring the group differences of the PAIS-SR subscales, significant differences were found in terms of the Sexual Relations (SR) and Social Environment (SE) subscales of the PAIS-SR ( $p<0.001$  and  $p=0.010$  respectively). When a statistically significant difference between groups was observed for the Total T score, as well as the PAIS-SR subscales, pairwise comparisons evaluated between each pair of groups using least-squares means. Regarding the Sexual Relations (SR) subscale, the 6-months post-surgical control group was significantly better functioning than the post-chemotherapy group ( $p<0.001$ ) and the pre-chemotherapy group ( $p=0.001$ ). Regarding the Social Environment (SE) subscale, the 6-months post-surgery group was significantly better functioning than the pre-chemotherapy group ( $p=0.033$ ) and the post-chemotherapy group ( $p=0.001$ ). The post-chemotherapy and the post-surgical groups also significantly differed ( $p=0.015$ ), with the post-surgical group having higher functioning.

Table 6: Median (Ranges) for Total PAIS-SR and Subscale T-Scores

	Total Sample	Group A (Pre-Chemo)	Group B (Post-Surgery Control)	Group C (Post-Chemo)	Group D (6-Months Post-Surgery Control)	p-value <sup>2</sup>
N	74	19	18	20	17	
Total T-Score	50 (23,75)	50 (23, 75)	45 (23, 70)	53 (34, 75)	44 (23, 63)	0.049
HCO T-Score <sup>1</sup>	48 (29, 75)	48 (29, 73)	47 (29, 60)	48 (35, 75)	46 (29, 63)	0.32
VE T-Score <sup>1</sup>	57 (43,76)	62 (45, 76)	56 (43, 70)	56 (45, 73)	52 (45, 67)	0.089
DE T-Score <sup>1</sup>	42 (34, 76)	49 (34, 69)	44 (34, 73)	47 (34, 76)	39 (34, 61)	0.10
SR T-Score <sup>1</sup>	53 (40, 76)	53 (40, 76)	51 (40, 72)	56 (47, 76)	43 (40, 74)	<0.001
EFR T-Score <sup>1</sup>	46 (46, 71)	46 (46, 71)	46 (46, 65)	52 (46, 71)	46 (46, 71)	0.45
SE T-Score <sup>1</sup>	47 (28, 66)	49 (28, 65)	46 (28, 59)	51 (28, 66)	45 (28, 55)	0.010
PD T-Score <sup>1</sup>	46 (34, 73)	46 (34, 73)	48 (34, 67)	46 (34, 72)	44 (34, 70)	0.94

<sup>1</sup> = PAIS-SR domains: Health Care Orientation (HCO); Vocational Environment (VE); Domestic Environment (DE); Sexual Relationships (SR); Extended Family Relationships (EFR); Social Environment SE); and Psychological Distress (PD).

<sup>2</sup> = Applies only to the pair-wise comparisons of Groups A thru D. Does not include Total Sample results.

### *Quality of Life*

The FACT-G and subscale scores are reported for the total sample and groups in Table 7. Differences between groups were compared for the FACT-G and subscales using the Kruskal-Wallis test. The between-group differences in the global FACT-G scores were statistically significant ( $p=0.028$ ). More specifically, it was the post-chemotherapy and 6-months post-surgery control groups' scores that significantly

differed ( $p=0.010$ ), with the 6-month post-surgical control having the higher quality of life.

When comparing groups, significant differences were found in the scores of the Physical Well-Being (PWB) and Social Well-Being sub-scales ( $p\text{-value} = 0.037$  and  $0.042$  respectfully). Within the Physical Well-Being subscale (PWB), the post-chemotherapy group significantly differed from the pre-chemotherapy group ( $p=0.031$ ) and the 6-months post-surgical group ( $p=0.012$ ), with the 6-month post-surgical controls having the highest quality of life and the post-chemotherapy group having the lowest quality of life. Within the Social Well-Being subscale, the post-chemotherapy group differed from the 6-months post-surgical group ( $p=0.003$ ), again with the 6-month post-surgical control group having the higher quality of life scores.

Table 7: Median (Ranges) for FACT-G and Subscale Scores

	Total Sample	Group A (Pre-Chemo)	Group B (Post-Surgery Control)	Group C (Post-Chemo)	Group D (6-Months Post-Surgery Control)	p-value <sup>2</sup>
N	72	19	18	20	13	
FACT-G	83.8 (36.1, 100)	87 (36, 98)	81 (59, 98)	76 (43, 95)	90 (56, 100)	0.028
PWB <sup>1</sup>	90.5 (17.9, 100)	96 (18, 100)	89 (57, 100)	80 (25, 100)	93 (61, 100)	0.037
SWB <sup>1</sup>	85.7 (14.3, 100)	86 (50, 100)	86 (57, 100)	81 (14, 100)	96 (71, 100)	0.042
EWB <sup>1</sup>	87.5 (25.0, 100)	85 (25, 100)	83 (46, 100)	85 (42, 100)	92 (33, 100)	0.69
FWB <sup>1</sup>	75.0 (14.3, 100)	79 (39, 100)	75 (14, 100)	68 (32, 100)	89 (36, 100)	0.16

1 = FACT-G subscales: Physical Well-Being (PWB); Social Well-Being (SWB); Emotional Well-Being (EWB); and Functional Well-Being (FWB).

2 = Applies only to the pair-wise comparisons of Groups A thru D. Does not include Total Sample results.

### *Research Questions*

Potential associations between PAIS, CANTAB and FACT-G were evaluated along with the effect of group. Using a linear regression model with PAIS total T score as the outcome and CANTAB Z-score as the predictor, the interaction effect between CANTAB Z-score and group was not significant ( $p = 0.56$ ) nor was the effect of group as a factor ( $p = 0.16$ ). This process was repeated for each CANTAB subscale and neither group nor interaction was a significant predictor of outcome for any subscale value. Thus, one can infer that the effect on PAIS by CANTAB is unaffected by the patient group.

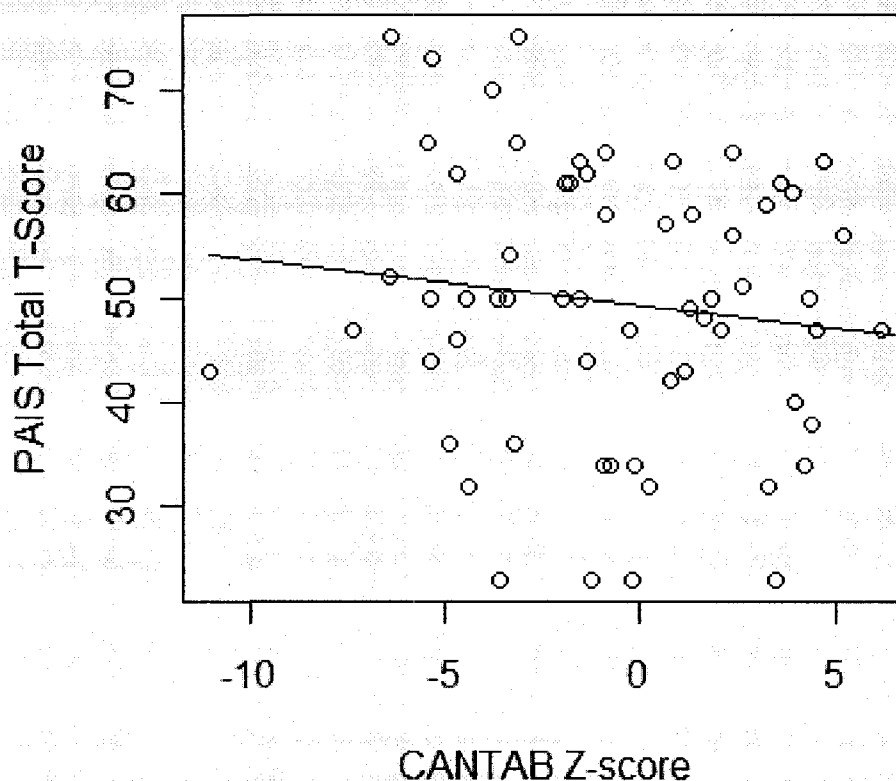
Similarly, the association between PAIS total T score and FACT-G score is unaffected by group when examined as part of an exploratory analysis (interaction  $p = 0.27$  and group factor  $p = 0.31$ ). As a result, associations between PAIS total T score with CANTAB and FACT-G were evaluated after combining all patients into a single group. Each score (PAIS, CANTAB and FACT-G) was approximately normal, thus, parametric estimates are appropriate and the Pearson correlation coefficient was used to estimate the association between these three factors. These results were used to answer Research Questions 1 and 3.

*1. What impact does adjuvant chemotherapy-induced cognitive dysfunction have upon the colorectal cancer patient's psychosocial adjustment?*

The Pearson correlation coefficient between PAIS Total T score and CANTAB Z-score was found to be -0.12 (95% confidence interval = -0.36 to 0.13,  $p = 0.33$ ) (see Figure 2). This result was not statistically significant. There was also no difference ( $p = 0.52$  using a Wilcoxon ranksum test) in PAIS Total T score between those scored as

having a deficit via CANTAB (mean score = 51.8) and those scored as not having a global deficit via CANTAB (mean score = 48.8).

Figure 2: Association Between PAIS-SR and CANTAB



*2. Does psychosocial adjustment differ between people diagnosed with colorectal cancer who do and do not receive adjuvant chemotherapy?*

Significant differences were found between groups in terms of PAIS-SR total T score ( $p = 0.049$ ) and for the Sexual Relations ( $p < 0.001$ ) and Social Environment ( $p = 0.010$ ) subscales. Pair-wise comparisons found that the post-chemotherapy group significantly differed from the 6-months post-surgical group in the PAIS-SR total T score ( $p = 0.008$ ), with the 6-month post-surgical controls having higher functioning. In terms

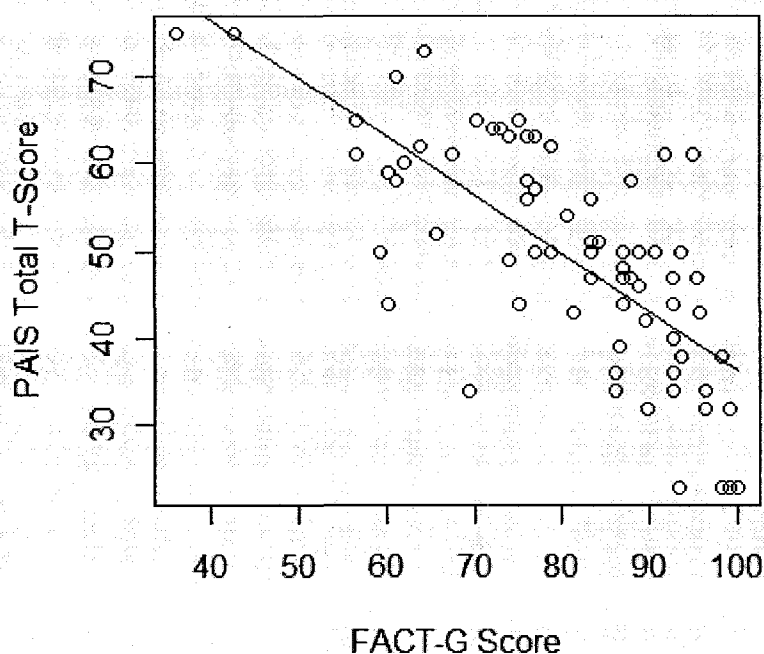


of the Sexual Relations subscale, the 6-months post-surgical group had significantly higher functioning than the pre-chemotherapy group ( $p = 0.001$ ) and the post-chemotherapy group ( $p < 0.001$ ). In terms of the Social Environment subscale, the 6-months post-surgical control group had significantly higher functioning than the pre-chemotherapy group ( $p = 0.033$ ), and the post-chemotherapy group ( $p < 0.001$ ), while the post-chemotherapy had significantly poorer functioning than the post-surgical group ( $p = 0.015$ ).

*3. What is the relationship between psychosocial adjustment and quality of life within a sample of colorectal cancer patients?*

There was a significant correlation between the PAIS Total T score and the FACT-G ( $r = -0.73$ ,  $CI = -0.82$  to  $-0.59$ ,  $p < 0.001$ ) (see Figure 3). For exploratory purposes, there was a weak, positive association found between FACT-G and CANTAB Z-score ( $r = 0.16$ ,  $CI = -0.09$  to  $0.39$ ,  $p = 0.21$ ).

Figure 3: Association Between PAIS-SR and FACT-G



## Chapter V

### *Discussion*

This correlational design allowed an exploration into the impact that chemotherapy-induced cognitive impairment has upon the non-metastatic colorectal cancer patient's psychosocial adjustment and quality of life. This design was useful in that it only looked at colorectal cancer patients who had had surgery, the main difference being whether one had chemotherapy treatment or not. Using such a design has an advantage over using a healthy control group, since the characteristics affecting colorectal cancer patients' psychosocial adjustment (Greer, 1994; Harrison & Maguire, 1994; Northouse et al., 2000) and quality of life (Arndt et al., 2004; Cameron, 2005; Esnaola et al., 2002; Rauch et al., 2004; Trentham-Dietz et al., 2003) are unique.

In assessing cognitive function, this study was useful in that it looked at subsets of patients assessed prior to and after chemotherapy administration. For the most part, previous research into cognitive function has assessed cancer patients after commencing chemotherapy and some has even begun assessing patients after chemotherapy completion. These methods limit the study's findings to patient recall, and the level of patient functioning prior to treatment administration is unknown. This current study is useful in that colorectal cancer patients were assessed cross-sectionally at various time points in the disease and treatment trajectories.

### *Research Questions*

*1. What impact does adjuvant chemotherapy-induced cognitive dysfunction have upon the colorectal cancer patient's psychosocial adjustment?*

The weak, negative correlation between cognitive function (CANTAB) and psychosocial adjustment (PAIS-SR) is statistically non-significant. Additionally, the differences in Total PAIS-SR T-scores of those who did and did not have a cognitive deficit also indicate that cognitive impairment and psychosocial adjustment are not related. Therefore, if a true association between these variables does exist, it is unlikely to be sufficiently strong enough to be of much clinical significance.

It is interesting to note that no significant differences in cognitive function were seen between the groups for either the CANTAB score or individual tests. This finding corroborates with Bender et al. (2006) who found no differences between women with breast cancer who recently completed chemotherapy and a breast cancer control group. This study also concurs with Iconomou et al. (2004) who found that objective cognitive performance was not affected by the type of chemotherapy, the type of cancer, or disease

stage. Collectively, these findings suggest that neither treatment allocation or disease stage affect the non-metastatic cancer patient's cognitive function.

Of Iconomou et al.'s (2004) mixed cancer sample, 15% demonstrated cognitive impairment, which is slightly lower than the patients who were treated with chemotherapy in this study. This difference may be due to their heterogeneous cancer sample, which encompasses the issues of many cancer populations. This slight difference may also illuminate the unique needs of the colorectal cancer patient.

The median PAIS-SR Total T-score found in this study was similar to that found by Kelman (1997) in her study exploring psychosocial adjustment and colorectal cancer patients with an ostomy (50 and 46.5 respectively). When looking at the Total PAIS-SR scores among the groups, their differences approached statistical significance ( $p = 0.049$ ). However, it is important to note that none of the groups' median result indicated psychosocial maladjustment as defined by the Total T-score  $\geq 62$ . This could indicate that as a group, stage of disease, treatment allocation, and time from diagnosis do not affect the non-metastatic colorectal cancer patient's psychosocial adjustment.

## *2. Does psychosocial adjustment differ between people diagnosed with colorectal cancer who do and do not receive adjuvant chemotherapy?*

Psychosocial Adjustment, and specifically Sexual Relations and Social Environment, differ between groups of colorectal cancer patients who do and do not receive chemotherapy. These significant differences have been detailed previously.

When looking at the ranges of PAIS-SR Total T-scores for each group, it is clear that participants in each of the groups had results indicating psychosocial maladjustment. An exploration into the modes of each score found that 6 in Group A, 4 in Group B, 3 in Group C, and 1 in Group D indicated maladjustment ( $n = 19, 18, 20, 17$  and proportions

are 31.5%, 22%, 15% and 5.8% respectively). These modes and proportions are also of interest in that they may indicate that patients who receive chemotherapy have poorer psychosocial adjustment than those who do not receive chemo, but that as time goes by, both groups' psychosocial adjustment improve. This suggestion is strengthened by the statistically significant difference found between the post-chemotherapy and 6-month post-operative groups.

When attempting to compare the above results with the literature, it was difficult to find longitudinal studies assessing psychosocial adjustment over time in colorectal cancer patients receiving chemotherapy. However, the psychosocial adjustment of colorectal cancer patients having had surgery has been assessed over time. Although they claim that most (70%) of their sample did not receive chemotherapy, the study conducted by Northouse et al. (2000) focused on the psychosocial adjustment of patients for 1-year after colon surgery: no distinguishing analyses were made between the chemotherapy and non-chemotherapy patients. They found the poorest scores of psychosocial adjustment occurred within 2 months of diagnosis and then began to drop to near baseline levels at 1-year. Similarly, Bekkers et al. (1997) found that the psychosocial problems that occurred within the first four post-operative months were not demonstrated at 1-year after surgery. Bekkers et al. also found that the surgery alone, apart from a cancer diagnosis, was the largest contributor of psychosocial problems. Collectively, these studies show the negative effect that chemotherapy and/or disease severity, as well as the positive effect that duration since cancer treatment has upon the colorectal cancer patient's psychosocial adjustment.

Derogatis and Derogatis (1990) claim that the domain scores of the PAIS-SR provide an illustration relative to the benefits and burdens in the patient's adjustment and

may identify areas where increased attention can be directed on the part of the health care team. In reference to the Sexual Relations (SR) domain, the 6-months post-surgery group significantly differed from both chemotherapy groups. This finding also suggests the impact of cancer treatment upon the sexual relationships of colorectal cancer patients and provides strength to the importance of disease stage. Simply put, it appears that more advanced cancer requiring more aggressive treatments, more adversely affects the sexual relationships of colorectal cancer patients. When considering the treatment side-effects of these more aggressive treatments, it is easily plausible that the physiological manifestations of treatment affect these people's sexual interests and performance.

Significant differences within the Social Environment (SE) domain were found between the groups, with the post-chemotherapy group having highest scores for impairment within their social and leisure activities. Again, these scores may be related to the physiologic symptoms that occur with chemotherapy treatments, keeping patients away from social settings that they previously enjoyed.

For all subscales and the Total T score, the median score among the 6-months post-surgical control patients was lowest, indicating highest psychosocial functioning. As previously hypothesized, this may be related to the lower stage of disease and longer duration post cancer treatment. Conversely, for all domains except the Vocational Environment (VE) and Domestic Environment (DE), the median score amongst post-chemotherapy patients was highest, indicating lowest functioning. This shows the broad impact of chemotherapy upon a colorectal cancer patient's psychosocial adjustment, even after completing treatment. It is only the VE and DE that is more severely affected when beginning chemotherapy, which seems reasonable due to the uncertainty surrounding this time in the disease trajectory.

3. *What is the relationship between psychosocial adjustment and quality of life within a sample of colorectal cancer patients?*

The Pearson correlation coefficient for PAIS-SR Total T-score and FACT-G was estimated to be - 0.73, which was statistically significant. Munro (2001) defines a correlation of 0.70 - 0.89 as high. Since higher scores of the PAIS-SR indicate maladjustment, and higher scores of the FACT-G indicate better quality of life, a negative correlation indicates that the results of the tools are related. Therefore, from the results of this study sample, it can be inferred that a relationship exists between psychosocial adjustment and quality of life with a high degree of strength. Alternatively stated, those with fewer psychosocial problems report higher quality of life.

When comparing study groups, quality of life (FACT-G) scores were shown to be statistically significant ( $p$ -value = 0.028). Of particular interest, is the high median FACT-G scores of those commencing chemotherapy as well as the 6-month post-surgery control group although the range of scores in the 6-month post-operative control group were higher. There is no clarity to these differences found in the literature. When looking at the quality of life of patients with locally recurrent rectal cancer, Esnaola et al. (2002) found that disease status, being disease free or having residual disease, had no effect on quality of life ( $p$  = 0.2). This study could help explain this lack of difference between disease stages in this study.

Esnaola et al. (2002) also suggested a decline in quality of life scores during the first year after surgery. Although their analysis did not focus on the differences between those receiving and not chemotherapy, it is easily seen that 34 of the 45, or 75%, of the patients received chemotherapy. Their finding concurs with the median scores of the treatment groups in this study showing a higher FACT-G score prior to chemotherapy as compared

to after chemotherapy. An explanation of the rising median scores of the surgery only groups could be that the duration after cancer treatment, or surgery in this case, results in an increasing quality of life. It would have been interesting to note if this same finding would have been seen in the chemotherapy groups if this study had of assessed patients 6-months after their chemotherapy treatments.

Of the FACT-G subscales, the post chemotherapy group significantly differed from the other groups in terms of the Physical Well-Being ( $p = 0.037$ ) and Social Well-Being ( $p = 0.042$ ) subscales. These differences could possibly be explained by the physical side-effects that accumulate during chemotherapy for colorectal cancer and thus remove these patients from their previously enjoyed activities.

#### *Implications for Nursing*

Although no significant differences in cognitive function were seen between the groups for either the CANTAB score or individual tests, it is important for nurses to recognize that cognitive deficits were found in each of these treatment groups. Since these findings further generalize those that are found within the oncology literature, nurses need to know that cognitive disturbances can occur at any time in the disease or treatment trajectory, and thus assess and arrange for appropriate interventions. Due to nurses' frequent proximity to cancer patients, they are in a unique position to provide ongoing assessments of patients' cognitive performance while undergoing cancer treatment and follow-up. Although detailed neurocognitive testing is conducted by those with an extensive psychology background, nurses can be a patient's first step toward such testing and treatment of these difficulties. Further research into the development or institutional formatting of an existing assessment tool for chemotherapy induced



cognitive impairment would be useful for front-line nurses caring for cancer patients.

This would be a useful multi-disciplinary research project.

In terms of psychosocial adjustment, the results from this sample further generalize that found within the oncology literature. However, it is important to note that none of the treatment groups' median score showed mal-adjustment, but that in exploring the modes, those beginning chemotherapy had a higher proportion of maladjusted scores. This is useful for nurses so that they can more closely assess psychosocial adjustment when their patients begin chemotherapy. When looking at the median subscale scores for this group of patients, nursing assessments should be targeted toward factors relating to patients' sexual relationships and social environment. The items that Derogatis and Derogatis' (1990) list as variables of interest for each domain can be easily assessed during a patient assessment. An assessment into the cancer patient's sexual relationships would assess the patient's perceived quality of the interpersonal relationship, moving toward more specific issues about their interest, frequency, satisfaction and/or dysfunction (Derogatis & Derogatis, 1990). Their social environment assessment encompasses leisure interests and activities that they enjoy individually, with their family and as part of a larger social network (Derogatis & Derogatis, 1990). These assessments both open the door for patient expression of concerns that are infrequently assessed as part of mainstream practice. This dialogue allows for intervention suggestions and referral opportunities.

It is also useful to know that psychosocial adjustment and quality of life are related, as evidenced by the correlation in PAIS-SR and FACT-G scores. This could be useful for any future research projects, not only those related to nursing.

### *Implications for the Theory of Unpleasant Symptoms*

The Theory of Unpleasant Symptoms is useful to guide the understanding of chemotherapy-induced cognitive impairment upon the psychosocial adjustment and quality of life in colorectal cancer patients. The association between performance, or cognitive impairment as indicated by the CANTAB, and influencing factors, as indicated by the PAIS-SR and FACT-G results, was shown to be minimally present and statistically non-significant. The claim for interactions among the influencing factors is strengthened by the statistically significant association between the PAIS-SR and FACT-G. Therefore, this study shows mixed support for the concepts within the Theory of Unpleasant Symptoms. It is important to note that this theory does have usefulness although this study's findings were non-significant. Such findings warrant further usage of this theory within oncology research projects.

### *Limitations of the Study*

One seeming limitation of this study was to use a cross-sectional methodology. It is well known that prospective studies provide more useful information when looking for associations between variables. Therefore, assessing colorectal cancer patients for a duration of time, using serial assessments would have been a more beneficial model to answer the research questions of this study. Also related to the above limitation, a longitudinal, prospective study would be useful to assess the seeming importance of duration after a colorectal cancer patient's cancer treatment.

### *Conclusion*

In this subset of colorectal cancer patients, there appears to be a weak, negative association between cognitive impairment and psychosocial adjustment, however the level of association was not significant statistically. Thus, if there is a true association

between these variables, the association is unlikely to be sufficiently strong to be of much clinical significance.

In terms of psychosocial adjustment and treatment groups, the Total PAIS-SR T-scores reached statistical significance. Significant differences were found between the groups for the Sexual Relations, and Social Environment domains.

Regarding the association between the psychosocial adjustment and quality of life, there was an inversely strong relationship found between the measures indicating that fewer psychosocial problems resulted in a higher quality of life.

Although the cited limitations of this study are acknowledged, this study is useful for health care professionals working with cancer patients to understand chemotherapy-induced cognitive impairment, psychosocial adjustment and quality of life in colorectal cancer patients.

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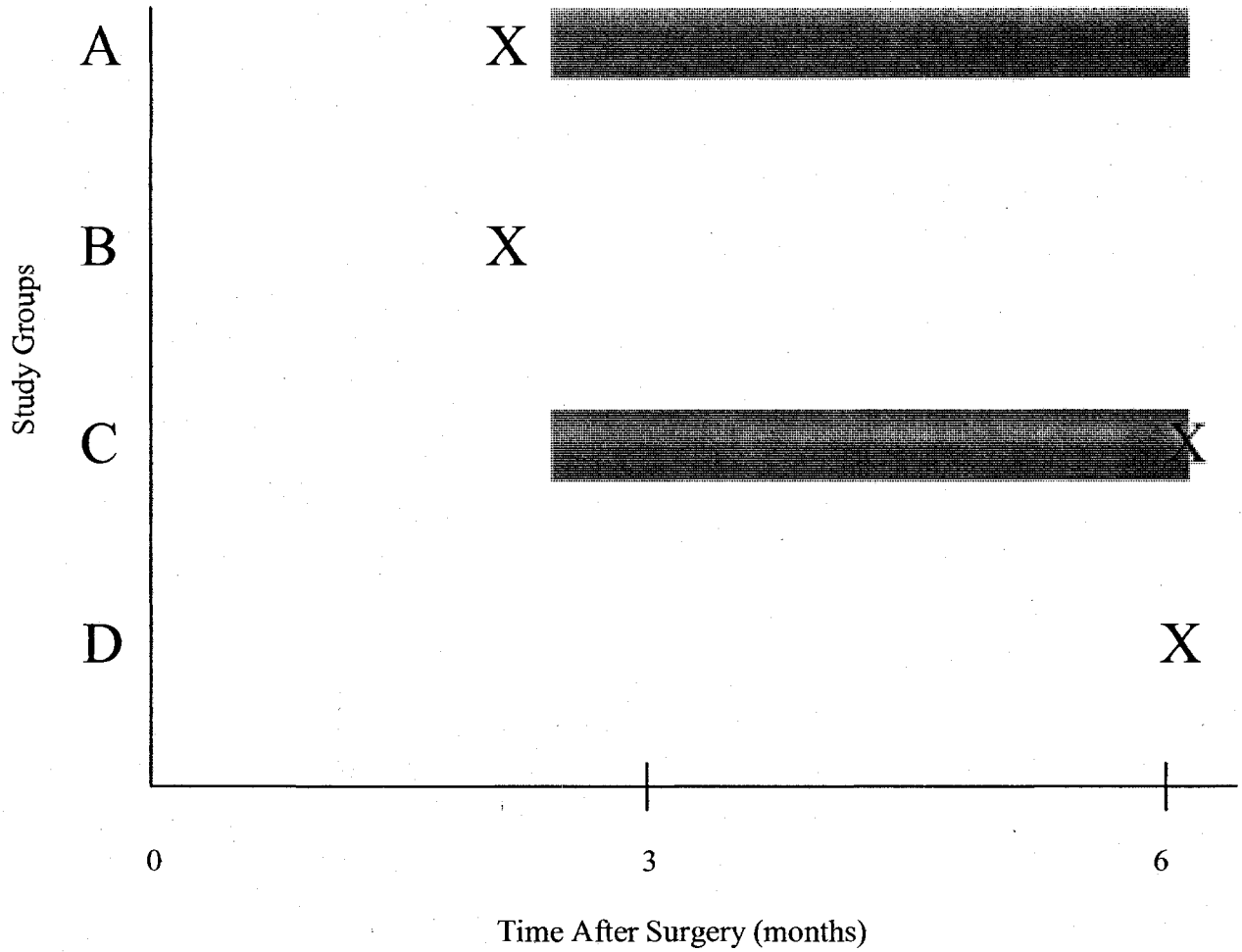


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## Appendix A

## Timing of Study Assessments

*Legend*

X Indicates administration of study measures

■ Indicates administration of adjuvant chemotherapy

## Appendix B - Consent Forms

**The Impact of Cognitive Dysfunction Upon the Non-Metastatic Colorectal Cancer  
Patient's Psychosocial Adjustment and Quality of Life**  
(For patients who will receive and who completed chemotherapy)

You are asked to participate in a research study conducted by Jacqueline Galica, a Graduate Student from the Faculty of Nursing at the University of Windsor, and her Principal Advisor, Dr. Deborah Kane, Associate Professor at the University of Windsor. The results of this study will be used to contribute to Jacqueline's thesis research within the Master of Science degree requirements.

Before agreeing to participate in this study, it is important that you read and understand the following explanation of the proposed study procedures. The following information describes the purpose, procedures, benefits, discomforts, risks and precautions associated with the study. It also describes your right to refuse to participate or withdraw from the study at any time. In order to decide whether you wish to participate in this research study, you should understand its risks and benefits to be able to make an informed decision. This is known as the informed consent process. Please ask the study staff to explain any words that you don't understand before signing this consent form. Make sure all of your questions have been answered to your satisfaction before signing this document.

**PURPOSE OF THE STUDY**

As a patient who will be receiving chemotherapy to try to prevent further problems from your bowel cancer, you have received information from your doctors about several possible side effects of treatment. You are participating in a study that will try to obtain information about side effects that might also occur as a result of your treatment, but which are often harder to measure. These possible side effects include tiredness, and subtle changes in your ability to think, concentrate, remember and react to things. You are now being asked to take part in another study that will try to determine how these side effects impact your personal and professional roles and functioning.

**PROCEDURES**

The study will involve completing a questionnaire in a quiet environment at your leisure. The approximate time that it takes to complete this questionnaire is 20-25 minutes. After completion, you will be asked to mail the completed questionnaire in the postage paid return address envelope. You will only be asked to complete this questionnaire one time. By consenting to this study, you are agreeing to allow the researcher to access your demographics and results of the cognitive assessment and questionnaires that you completed within the larger study that you are participating in.

**POTENTIAL RISKS AND BENEFITS TO SUBJECTS AND/OR TO SOCIETY**

There are no known risks associated with the study. It will not change your medical treatment in any way. There are also no direct benefits to you. The aim is to find out more information about side effects of chemotherapy. This information will be used to give better advice to patients like you who receive chemotherapy in the future.

If you become ill or are physically injured as a result of participation in this study, medical treatment will be provided. The reasonable costs of such treatment will be covered by your health insurance for any injury or illness that is directly a result of participation in this study. In no way does signing this consent form waive your legal rights nor does it relieve the investigators, sponsors or involved institutions from their legal and professional responsibilities.

#### **PAYMENT FOR PARTICIPATION**

You will not receive payment for your participation in this study. It is not expected that you should incur any expenses as a result of your participation.

#### **CONFIDENTIALITY**

All information obtained during this study will be held in strict confidence. You will be identified with a study number only. No names or identifying information will be used in any publication or presentations. No information identifying you will be transferred outside the investigators in this study or this hospital. The individual questionnaires and results will be destroyed after the study analysis has taken place.

#### **PARTICIPATION AND WITHDRAWAL**

Your participation in this study is voluntary. You can choose not to participate or you may withdraw at any time without affecting your medical care.

#### **FEEDBACK OF THE RESULTS OF THIS STUDY TO THE SUBJECTS**

Individual results will not be routinely given to participants. However, if participants would like to know the results of their assessment, they may contact the research investigator directly. Participants may also review the overall outcomes of the study in the 'Study Results' section on the University of Windsor's REB website at [www.uwindsor.ca/reb](http://www.uwindsor.ca/reb).

#### **RIGHTS OF RESEARCH SUBJECTS**

If you suffer any side effects or other injuries during the study, or if you have any general questions about the study, please call the person in charge of this study, Jacqueline Galica at (416) 946-4501 extension 3176.

If you have questions about your rights as a research participant, please call Dr. R. Heslegrave, Chair of the University Health Network Research Ethics Board at (416) 340-4557. You may also contact the Research Ethics Coordinator at the University of Windsor, (519) 253-3000 extension 3916. These people are not involved with the research project in any way and calling them will not affect your participation in the study.

#### **SIGNATURE OF RESEARCH SUBJECT/LEGAL REPRESENTATIVE**

I have had the opportunity to discuss this study and my questions have been answered to my satisfaction. I consent to take part in the study with the understanding that I may withdraw at any time without affecting my medical care. I have received a signed copy of this consent form. I voluntarily consent to participate in this study.

_____	_____	_____
Study Subject's Name (Please Print)	Study Subject's Signature	Date

**SIGNATURE OF INVESTIGATOR**

I confirm that I have explained the nature and purpose of the study to the subject named above. I have answered all questions.

_____	_____	_____
Name of Person Obtaining Consent	Signature	Date



**The Impact of Cognitive Dysfunction Upon the Non-Metastatic Colorectal Cancer  
Patient's Psychosocial Adjustment and Quality of Life**  
(For patients who do not need chemotherapy)

You are asked to participate in a research study conducted by Jacqueline Galica, a Graduate Student from the Faculty of Nursing at the University of Windsor, and her Principal Advisor, Dr. Deborah Kane, Associate Professor. The results of this study will be used to contribute to Jacqueline's thesis research within the Master of Science degree requirements.

Before agreeing to participate in this study, it is important that you read and understand the following explanation of the proposed study procedures. The following information describes the purpose, procedures, benefits, discomforts, risks and precautions associated with the study. It also describes your right to refuse to participate or withdraw from the study at any time. In order to decide whether you wish to participate in this research study, you should understand its risks and benefits to be able to make an informed decision. This is known as the informed consent process. Please ask the study staff to explain any words that you don't understand before signing this consent form. Make sure all of your questions have been answered to your satisfaction before signing this document.

**PURPOSE OF THE STUDY**

As a patient who has been diagnosed with bowel cancer and has had surgery for this, but who either does not need to have chemotherapy or does not wish to have chemotherapy, you have been asked to participate in a study that will try to obtain information about side effects of chemotherapy. These include tiredness, and subtle changes in the ability to think, concentrate, remember and react to things. You are now being asked to take part in another study that will try to determine how these side effects impact patients' personal and professional roles and functioning.

**PROCEDURES**

The study will involve completing a questionnaire in a quiet environment at your leisure. The approximate time that it takes to complete this questionnaire is 20-25 minutes. After completion, you will be asked to mail the completed questionnaire in the postage paid return address envelope. You will only be asked to complete this questionnaire one time. By consenting to this study, you are agreeing to allow the researcher to access your demographics and results of the cognitive assessment and questionnaires that you completed within the larger study that you are participating in.

**POTENTIAL RISKS AND BENEFITS TO SUBJECTS AND/OR TO SOCIETY**

There are no known risks associated with the study. It will not change your medical treatment in any way. There are also no direct benefits to you. The aim is to find out more information about side effects of chemotherapy. This information will be used to give better advice to patients like you who receive chemotherapy in the future.

If you become ill or are physically injured as a result of participation in this study, medical treatment will be provided. The reasonable costs of such treatment will be covered by your health insurance for any injury or illness that is directly a result of participation in this study. In no way does signing this consent form waive your legal rights nor does it relieve the investigators, sponsors or involved institutions from their legal and professional responsibilities.

#### **PAYMENT FOR PARTICIPATION**

You will not receive payment for your participation in this study. It is not expected that you should incur any expenses as a result of your participation.

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All information obtained during this study will be held in strict confidence. You will be identified with a study number only. No names or identifying information will be used in any publication or presentations. No information identifying you will be transferred outside the investigators in this study or this hospital. The individual questionnaires and results will be destroyed after the study analysis has taken place.

#### **PARTICIPATION AND WITHDRAWAL**

Your participation in this study is voluntary. You can choose not to participate or you may withdraw at any time without affecting your medical care.

#### **FEEDBACK OF THE RESULTS OF THIS STUDY TO THE SUBJECTS**

Individual results will not be routinely given to participants. However, if participants would like to know the results of their assessment or study, they may contact the research investigator directly. Participants may also review the overall outcomes of the study in the 'Study Results' section on the University of Windsor's REB website at [www.uwindsor.ca/reb](http://www.uwindsor.ca/reb).

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#### **SIGNATURE OF RESEARCH SUBJECT/LEGAL REPRESENTATIVE**

I have had the opportunity to discuss this study and my questions have been answered to my satisfaction. I consent to take part in the study with the understanding that I may withdraw at any time without affecting my medical care. I have received a signed copy of this consent form. I voluntarily consent to participate in this study.

\_\_\_\_\_  
Study Subject's Name (Please Print)

\_\_\_\_\_  
Study Subject's Signature

\_\_\_\_\_  
Date

**SIGNATURE OF INVESTIGATOR**

I confirm that I have explained the nature and purpose of the study to the subject named above. I have answered all questions.

\_\_\_\_\_  
Name of Person  
Obtaining Consent

\_\_\_\_\_  
Signature

\_\_\_\_\_  
Date

## Appendix C – CANTABclipse Test Descriptions

Test Name	Duration	Purpose
<b>Screening Tests</b>		
Motor Screening (MOT)	3 minutes	Designed to relax the participant and introduce them to the computer and touch screen. Screens for visual, movement and comprehension difficulties.
Big/Little Circle (BLC)	3 minutes	A test of following a simple rule and then reversing it. Assess comprehension learning and reversal.
<b>Visual Memory Tests</b>		
Delayed Matching to Sample (DMS)	10 minutes	Tests simultaneous and delayed matching to a sample. Sensitive to damage in the medial temporal lobe, with some input from the frontal lobes.
Paired Associates Learning (PAL)	10 minutes	Assesses visual memory and new learning.
Pattern Recognition Memory (PRM)	5 minutes	Assesses the ability to recognize a previously viewed pattern.
Spatial Recognition Memory (SRM)	5 minutes	A test of spatial recognition memory where the subject tries to remember where which object is located in the location where it was previously seen.
<b>Working Memory and Planning Tests</b>		
Stockings of Cambridge (SOC)	10 minutes	A test where the subject is to copy a given pattern. Assesses spatial planning and motor control.
Spatial Span (SSP)	5 minutes	Assesses working memory capacity whereby the subject touches a sequence of objects in the same order that they were presented.
Spatial Working Memory (SWM)	8 minutes	Tests ability to retain spatial information and manipulate remembered items in working memory.
Intra-Extra Dimensional Set Shifting (IED)	7 minutes	A test of rule acquisition and reversal. Assesses visual discrimination and flexibility and shifting of attention.
Match to Sample Visual Search (MTS)	9 minutes	Tests the ability of matching visual stimuli while measuring reaction and movement time
Reaction Time (RTI)	5 minutes	Measures the speed of response to a visual target where the stimulus is either predictable or unpredictable.
Rapid Visual Information Processing (RVP)	7 minutes	Tests visual sustained memory. Subjects are given 3 number sequences to remember and then press a touch pad when a sequence appears.
<b>Additional Tests</b>		
Affective Go/No-go (AGN)	10 minutes	A series of words are flashed on the screen and subjects touch pad when a word of an indicated valence (positive, negative or neutral) is shown.
Verbal Recognition Memory (VRM)	20 minutes (2 modes)	Assesses immediate and delayed memory of verbal information by remembering as many presented words as possible and then indicating previously presented words in a subsequent presentation.

**Appendix D - Psychosocial Adjustment to Illness Scale – Self Report Version (PAIS-SR)**  
**Sample Items**

Psychosocial Adjustment to Illness Scale – Self Report Version (PAIS-SR) Sample Items  
 Copyright 1978, 1983 by Leonard R. Deogatis, PhD

### **INSTRUCTIONS**

The present form contains questions concerning the effects that your illness has had on you. We are interested in knowing what effects it has had on your relationships and your ability to perform at home and on your job. Also, we would like to know about the effects on family and personal relationships. Other questions concern its effect on your social and leisure time activities, and how you have felt emotionally.

In answering each question, please put a check mark (✓) in the box alongside the answer that best describes your experience. Please answer all the questions and try not to skip any. If none of the answers to a question match your experience exactly, please choose the answer that comes closest to the experience you have had.

The time we would like to refer to is **the past 30 days, including today**. Answer each question in terms of what your experience has been like during this time frame. In the event you are presently a patient in the hospital, please report your experiences for **the 30 days before entering the hospital**.

Some questions on the form assume that you are married or have a steady partner you are close to. Other questions ask about family relationships. If these questions do not apply to you because you are unmarried, or you have no family or partner, please leave them blank. Try to answer **all** the questions that do apply to you, however.

Section II asks questions about your job performance. If you have either full-time or substantial part-time employment, please answer in terms of your job. If you are primarily a student, answer in terms of your **schoolwork**. If you are a housewife, answer as though **housework**, neighbours, etc. are your work environment.

-----

We appreciate the time you have taken to do this form. Please check again to make sure you have completed all the items. If you have any questions about this form, please ask. If you are responding by mail, please write them in the space provided below. Please return the form as soon as you've completed it.

Thank You.

---

(Copyright and trademark laws do not permit the reproduction of the complete Psychosocial Adjustment to Illness Scale. The following sample items are provided.)

**SECTION I**

**(1) Which of the following statements best describes your usual attitude about taking care of your health?**

- ☐ a) I am very concerned and pay close attention to my personal health.
- ☐ b) Most of the time I pay attention to my health care needs.
- ☐ c) Usually, I try to take care of health matters but sometimes I just don't get around to it.
- ☐ d) Health care is something that I just don't worry too much about.

**(2) Your present illness probably requires some special attention and care on your part. Would you please select the statement below that best describes your reaction.**

- ☐ a) I do things pretty much the way I always have done them and I don't worry or take any special considerations for my illness.
- ☐ b) I try to do all the things I am supposed to do to take care of myself, but lots of times I forget or I am too tired or busy.
- ☐ c) I do a pretty good job taking care of my present illness.
- ☐ d) I pay close attention to all the needs of my present illness and do everything I can to take care of myself.

**SECTION II**

**(1) Has your illness interfered with your ability to do your job (schoolwork)?**

- ☐ a) No problems with my job
- ☐ b) Some problems, but only minor ones
- ☐ c) Some serious problems
- ☐ d) Illness has totally prevented me from doing my job

**(2) How well do you physically perform your job (studies) now?**

- ☐ a) Poorly
- ☐ b) Not too well
- ☐ c) Adequately
- ☐ d) Very well



### **SECTION III**

**(1) How would you describe your relationship with your husband or wife (partner, if not married) since your illness?**

- [   ]     a) Good
- [   ]     b) Fair
- [   ]     c) Poor
- [   ]     d) Very Poor

**(2) How would you describe your general relationships with other people you live with (e.g., children, parents, aunts, etc.)?**

- [   ]     a) Very Poor
- [   ]     b) Poor
- [   ]     c) Fair
- [   ]     d) Good

### **SECTION IV**

**(1) Sometimes having an illness can cause problems in a relationships. Has your illness led to any problems with your husband or wife (partner, if not married)?**

- [   ]     a) There has been no change in our relationship
- [   ]     b) We are a little less close since my illness
- [   ]     c) We are definitely less close since my illness
- [   ]     d) We have had serious problems or a break in our relationship since my illness

**(2) Sometimes when people are ill they report a loss of interest in sexual activities. Have you experienced less sexual interest since your illness?**

- [   ]     a) Absolutely no sexual interest since illness
- [   ]     b) A marked loss of sexual interest
- [   ]     c) A slight loss of sexual interest
- [   ]     d) No loss of sexual interest

**SECTION V**

**(1) Have you had as much contact as usual (either personally or by telephone) with members of your family outside your household since your illness?**

- ☐ ☐ a) Contact is the same or greater since illness  
☐ ☐ b) Contact is slightly less  
☐ ☐ c) Contact is markedly less  
☐ ☐ d) No contact since illness

**(2) Have you remained as interested in getting together with these numbers of your family since your illness?**

- ☐ ☐ a) Little or no interest in getting together with them  
☐ ☐ b) Interest is a lot less than before  
☐ ☐ c) Interest is slightly less  
☐ ☐ d) Interest is the same or greater since illness

**SECTION VI**

**(1) Are you still as interested in your leisure time activities and hobbies as you were prior to your illness?**

- ☐ ☐ a) Same level of interest as previously  
☐ ☐ b) Slightly less interest than before  
☐ ☐ c) Significantly less interest than before  
☐ ☐ d) Little or no interest remaining

**(2) How about actual participation? Are you still actively involved in doing those activities?**

- ☐ ☐ a) Little or no participation at present  
☐ ☐ b) Participation reduced significantly  
☐ ☐ c) Participation reduced slightly  
☐ ☐ d) Participation remains unchanged

**SECTION VII**

**(1) Recently, have you felt afraid, tense, nervous, or anxious?**

- ☐ ☐ a) Not at all   ☐ ☐ b) A little bit   ☐ ☐ c) Quite a bit   ☐ ☐ d) Extremely

**(2) Recently, have you felt sad, depressed, lost interest in things, or felt hopeless?**

- ☐ ☐ a) Extremely   ☐ ☐ b) Quite a bit   ☐ ☐ c) A little bit   ☐ ☐ d) Not at all

**Appendix E: Functional Assessment to Cancer Therapy – General (FACT-G)**

## FACT-G (Version 4)

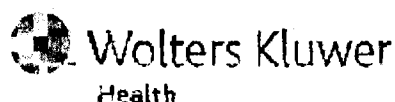
Below is a list of statements that other people with your illness have said are important. By **circling one (1) number per line**, please indicate how true each statement has been for you **during the past 7 days**.

PHYSICAL WELL-BEING		Not at all	A little bit	Some- what	Quite a bit	Very much
GP1	I have a lack of energy .....	0	1	2	3	4
GP2	I have nausea .....	0	1	2	3	4
GP3	Because of my physical condition, I have trouble meeting the needs of my family...	0	1	2	3	4
GP4	I have pain .....	0	1	2	3	4
GP5	I am bothered by side effects of treatment .....	0	1	2	3	4
GP6	I feel ill .....	0	1	2	3	4
GP7	I am forced to spend time in bed.....	0	1	2	3	4
SOCIAL/FAMILY WELL-BEING		Not at all	A little bit	Some- what	Quite a bit	Very much
GS1	I feel close to my friends .....	0	1	2	3	4
GS2	I get emotional support from my family ....	0	1	2	3	4
GS3	I get support from my friends.....	0	1	2	3	4
GS4	My family has accepted my illness .....	0	1	2	3	4
GS5	I am satisfied with family communication about my illness.....	0	1	2	3	4
GS6	I feel close to my partner (or the person who is my main support) .....	0	1	2	3	4
Q1	Regardless of your current level of sexual activity, please answer the following question. If you prefer not to answer it, please check this box <input type="checkbox"/> and go to the next section.					
GS7	I am satisfied with my sex life	0	1	2	3	4

By circling one (1) number per line, please indicate how true each statement has been for you during the past 7 days.

EMOTIONAL WELL-BEING		Not at all	A little bit	Some- what	Quite a bit	Very much
GE1	I feel sad.....	0	1	2	3	4
GE2	I am satisfied with how I am coping with my illness.....	0	1	2	3	4
GE3	I am losing hope in the fight against my illness.....	0	1	2	3	4
GE4	I feel nervous .....	0	1	2	3	4
GE5	I worry about dying .....	0	1	2	3	4
GE6	I worry that my condition will get worse ...	0	1	2	3	4
FUNCTIONAL WELL-BEING		Not at all	A little bit	Some- what	Quite a bit	Very much
GF1	I am able to work (include work at home).....	0	1	2	3	4
GF2	My work (include work at home) is fulfilling.....	0	1	2	3	4
GF3	I am able to enjoy life .....	0	1	2	3	4
GF4	I have accepted my illness.....	0	1	2	3	4
GF5	I am sleeping well.....	0	1	2	3	4
GF6	I am enjoying the things I usually do for fun .....	0	1	2	3	4
GF7	I am content with the quality of my life right now .....	0	1	2	3	4

## Appendix F: Letters of Permission



Lippincott Williams & Wilkins  
351 W. Camden Street  
Philadelphia, PA 19104

410 528 4000 ext  
www.LWW.com

DATE: 09/22/08

Jacqueline Galica, RN, BScN, MSc(c)

Fee: \$0.00

Re: *Advances in Nursing Science*  
Spec Mtr: ANS, 1997, 19(3), 14-27, Fig. 2.  
Thesis use/ non-commercial

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**From:** David Hart [David.Hart@camcog.com]

**Sent:** Wednesday, August 13, 2008 5:25 AM

**To:** Galica, Jacqueline

**Subject:** re: CANTAB information

Dear Jacqueline,

Thank you for the email. With regard to using CANTAB, the gold standard CANTABeclipse (see datasheet above for details) package for academic research is currently the complete portable CANTABeclipse 10-year system which is available as standard at a total (ex-works) cost of £10,200. This provides unlimited use over a 10-year period of the full suite of twenty-two CANTAB tests running on the standardised lightweight portable SlimBook panel touchscreen PC. The software includes the child and adult test versions, parallel forms, child and adult normative databases, software user and test administration manuals, software key, 3 months technical support and a free training placement on one of the CANTABeclipse administrator training days in Cambridge. These systems are dispatched fully commissioned with all of the CANTABeclipse and platform software so that following delivery testing can begin immediately on power-up.

The 10-year CANTABeclipse software can be purchased without any hardware at £7,700 per site (a 'site' is a single PC running the software for testing subjects). Clip-on touchscreens for desktop monitors and laptop screens can be provided by CCL from £275 if necessary.

If the 10-year software is too expensive for the budget or simply provides more than your study protocol requires, then either the CANTABeclipse 1-year custom software, the CANTABeclipse 1-year modular software or the CANTABeclipse 4-year modular software may be more attractive options. These provide the same features and benefits as the 10-year software but at a lower cost based on a shorter licence period and access to fewer tests - either individual tests (with the custom licence) or seven tests (with the modular licence) cherry-picked from the full battery of twenty-two.

With the SlimBook touchscreen PC included, the standard full system cost is currently £3,250 (one test) to £4,000 (four tests) for the 1-year custom option, and £4,100 (1-year) to 7,200 (4-year) for the seven test modular option. Without the hardware, the cost is £750 to £1,500 for the 1-year custom software, and £1,600 to £4,700 for the modular versions. The custom and modular software licences include the associated child and adult test versions as well as parallel forms depending on which tests are selected, child and adult normative databases, software user and test administration manuals, software key and 3 months technical support.

I hope this information helps with regard to using CANTAB with your masters thesis. Please do not hesitate to contact us if we are able to provide additional details or you have any queries.

With very best wishes

David

**David T Hart**

Business Development Manager  
Academic Research (UK and ROW)  
Cambridge Cognition Ltd

tel: +44 (0) 1223 810700

fax: +44 (0) 1223 810701

mobile: +44 (0) 7899 790762

email: david.hart@camcog.com

web: [www.cantab.com](http://www.cantab.com)



**From:** MDero@aol.com  
**Sent:** Monday, September 19, 2005 3:59 PM  
**To:** Galica, Jacqueline  
**Subject:** PAIS-SR Instrument  
Dear Ms. Galica,

We recently received an e-mail from you concerning credentials necessary for using the PAIS-SR. Because you are doing your thesis and will have an advisor/supervisor working with you, you definitely will qualify to use the PAIS-SR.

Once you have completed and submitted a Qualification form from our Log In button on our website, [www.derogatis-tests.com](http://www.derogatis-tests.com), we will provide you with a User ID and password and you can order directly from our website.

If you have any questions concerning this process, please do not hesitate to contact me.

Sincerely,  
[MDero@aol.com](mailto:MDero@aol.com)

**From:** MDero@aol.com  
**Sent:** Wednesday, December 14, 2005 9:54 AM  
**To:** Galica, Jacqueline  
**Subject:** Re: PAIS-SR Instrument Publication Guidelines  
December 14, 2005

Dear Ms. Galica,

Our guidelines are, - you can include up to 2 sample items from each of the PAIS-SR domains. We do not allow reproductions of the entire scale in any publications. Thank you for checking with us concerning this matter.

If you have any further questions, please do not hesitate to contact us.

Sincerely,  
MDerogatis



## Functional Assessment of Chronic Illness Therapy

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### VITA AUCTORIS

Jacqueline Patricia Galica was born in 1977 in Toronto, Ontario. She graduated from Norwood District High School in 1996. From there, she went on to Ryerson Polytechnic University where she obtained a Bachelor of Science in Nursing in 2000. She is currently a candidate for the Master of Science in Nursing degree at the University of Windsor and hopes to graduate in Fall 2008.